HYPERPIESIA
AND
HYPERPIESIS

H. BATTY SHAW

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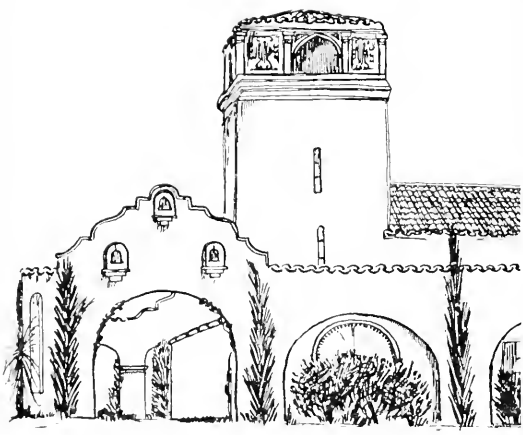
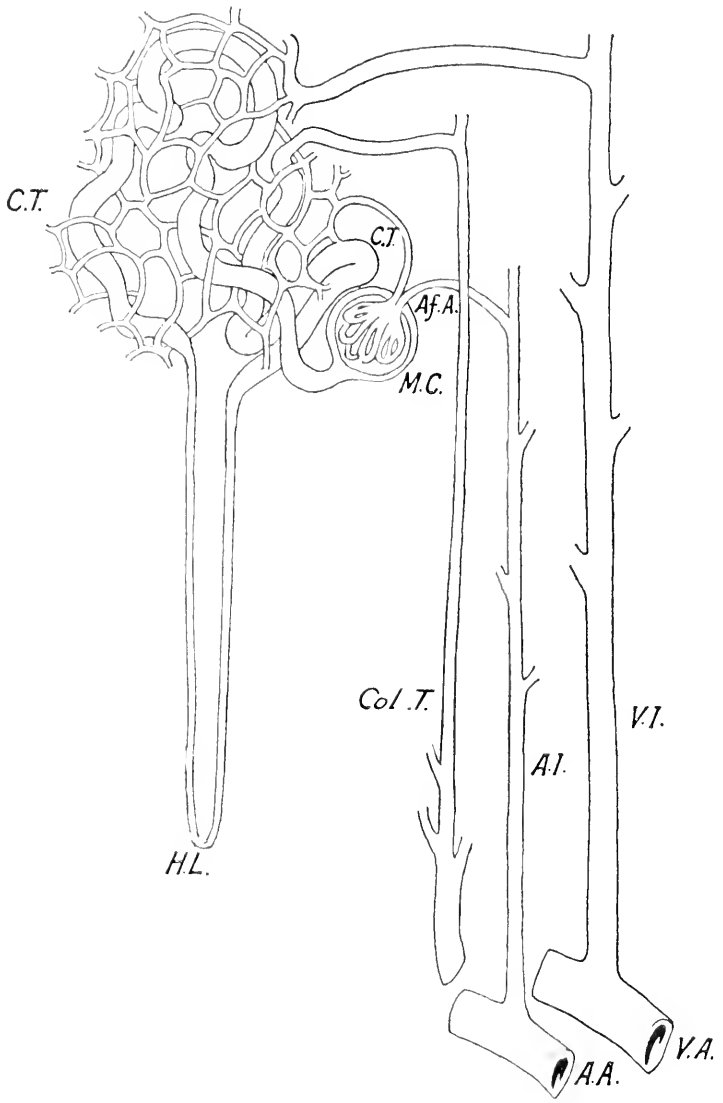


HYPERPIESIA AND HYPERPIESIS

(HYPERTENSION)



A.A. Arteria Arciformis.
V.A. Vena ,, .
A.I. Art. interlobularis.
V.I. Vena ,, .
Af.A. Afferent arteriole.
M.C. Malpighian Corpuscle (showing capillary tuft and Bowman's capsule).
C.T. Convoluted Tubule.
H.L. Loop of Henle
Col.T. Collecting Tubule.

FIG. 1.—Diagram of the vascular supply of the Kidney, showing how both convoluted tubules are brought under the influence of the blood after the latter has left the Malpighian Corpuscle.

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HYPERPIESIA

AND

HYPERPIESIS

(HYPERTENSION)

A Clinical, Pathological & Experimental Study

BY

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"For ease and speed in doing a thing do not give the work lasting solidity or exactness of beauty."

PLUTARCH'S *Life of Fabius*

LONDON
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TO

RT. HON. SIR CLIFFORD ALLBUTT, P.C., M.A., M.D., F.R.C.P., K.C.B.,

REGIUS PROFESSOR OF PHYSIC IN THE UNIVERSITY OF CAMBRIDGE,

TO WHOM IS OWING THE CLINICAL CONCEPTION UPON WHICH

THIS STUDY IS BASED.

CONTENTS

SECTION III

SECTION IV

SECTION V

LIST OF ILLUSTRATIONS

FIGURES

FIGS. 1–10 (FROM DRAWINGS BY MR. T. W. P. LAWRENCE).

SCHEME

CHARTS

TABLES

HYPERPIESIA

GENERAL INTRODUCTION

THE subject of Hyperpiesia, to use a term introduced by Sir Clifford Allbutt, is one of theoretical interest and of practical importance. The consideration of the cause of Hyperpiesia has led to much speculation and investigation, just as was the case when fever began to be studied by means of the clinical thermometer. Difficulties arose as to the explanation of the occurrence of fever ; there were those who considered that fever might be but an expression of individual physiological peculiarity—the febrile patient was merely one in whom metabolic change was more brisk than in others. It was also found experimentally that certain parts of the central nervous system were apparently set aside for the control of the loss or retention of body heat, and it was recognised that hæmorrhage into certain parts of the brain and bulb was capable of causing a rise of temperature. The mechanical explanations of rise of temperature were not adequate, and by the help of bacteriology it was recognised that fever connoted in many instances the toxic effect of fever-producing substances ; mechanical causes and physiological peculiarities gave large place to chemical agencies derived from micro-organisms.

In a similar way the cause or causes of Hyperpiesia have been held to be of a mechanical nature. The heart was considered to be endowed with powers of discernment which led to its overpowering of the resistance in the arterial bed, not only when generally contracted or narrowed by occlusive disease, but also when such change was restricted to a part only of the arterial system. As a corollary to this proposition, Hyperpiesia gradually became to be considered a mere function of ageing ; age led to the occlusion of the lumina of arteries, and this occlusion led to hypertension or hyperpiesis. The mechanical theory, however, could not withstand the criticism of those who were able to establish, thanks to the invention by Riva-Rocci of the sphygmomanometer, the existence of Hyperpiesia and of its sign hyperpiesis without any evidence of the existence of disease of the arteries which could lead to the reduction of their lumina. The escape from the difficulty was at hand, remembering the experience with regard to the oft-established toxic cause of fever, and a toxic origin of Hyperpiesia was invoked. Progress from this stage was, and has been slow for the simple reason that soluble pressor substances are few in number, and bacteriology has failed till

recently to demonstrate pressor toxic substances of microbic origin. So far the existence of pressor substances in the blood which are responsible for Hyperpiesia is largely a presumption, but is supported by strong circumstantial evidence.

A study has been made and presented in this volume with the object of showing to what extent kidney change is met with in Hyperpiesia, and the reason for this special inquiry is that hyperpiesis in the past has been considered to be a prerogative function of certain forms of kidney disease, a view which will be seen to be too narrow, if not quite erroneous.

The material upon which the study is based was afforded during several years by my colleagues at University College Hospital, to each of whom I offer my sincerest thanks.

The term Hyperpiesia has been introduced by Sir Clifford Allbutt to fix the identity of a pathological state which is free from any organic associations beyond cardiac hypertrophy and altered vessels; the blood-pressure is raised in this condition, that is to say hyperpiesis or hypertension is a sign of the disease—Hyperpiesia.

The number of cases showing hyperpiesis which came under consideration was large, and of these fifty had proved fatal when the study was brought to a conclusion. The first section of this volume contains an account of the clinical and post-mortem records of these cases.

The succeeding section contains an analysis of the results of these studies, and various deductions are made. Mr. T. W. P. LAWRENCE has added his investigations on the histological changes met with in the parenchyma and vessels of the kidneys, thereby greatly adding to my indebtedness to him for his help in this, as in other histological inquiries.

The third section refers to the various theories which have been put forward to explain hyperpiesis, and also the allied state of "idiopathic cardiac hypertrophy," and reasons are given for the view that some cases at least of hyperpiesis may be of renal origin.

This section is followed by the fourth, in which experimental evidence is given connected with renin and other substances which have been discovered to have a pressor effect. In this section reference is also made to the subject of anaphylaxis and its possible bearing upon the symptoms connected with Hyperpiesia.

In the last section there is a résumé of the findings in previous sections, and an account of Hyperpiesia as a disease *sui generis*. Hyperpiesia will be shown to figure in Medicine in much the same way as Eclampsia does in Gynæcology; the latter disease being recognised as a disease of unknown toxic origin. Reference is also made to the therapeutic management of Hyperpiesia.

Some of the problems dealt with in this volume have been objects of the closest study at the hands of members of the medical profession for many years. If little or no reference has been made to their individual labours, the writer begs

for allowance to be made for such treatment on the ground that this volume is not meant to be a bibliographical study, but aims at being a constructive effort which requires that older conceptions should be set aside at any rate for a period, so that the problems connected with Hyperpiesia should be viewed from an angle widely different from that one from which the subject has hitherto been considered. In Sir Clifford Allbutt's two volumes on *Diseases of the Arteries* a full bibliographical reference will be found.

The author cannot refrain from well-deserved expressions of gratitude to the sisters and nurses of University College Hospital, who through so many years have carried out observations on the blood-pressure of literally hundreds of patients—not observations for one day only, but, as the charts indicate, for many days. The records published in this volume are only those of cases who died: numerous other charts were drawn up of the blood-pressure readings of those who for purposes of control, never at any time showed hyperpiesis, and of those who showed hyperpiesis throughout their stay in the hospital or showed hyperpiesis for a time only, before they were discharged.

The author's best thanks are due to Miss E. L. Anderson, upon whose shoulders has fallen the task of helping to prepare the book for publication.

SECTION I

CLINICAL AND POST-MORTEM REPORTS

CASES were said to have hyperpiesis in whom the systolic blood-pressure, taken on the upper arm, during recumbency, registered 150 mm. or more. In some cases the number of observations was very limited, owing to the fact that the patients were seriously ill on admission, and died shortly afterwards. The majority of the cases were under much more protracted observation. The pressure varied, and in some cases fell below normal before death. In others it rose again before death, and in still others was maintained throughout the patient's stay. The observations were made at night and in the morning, and were checked repeatedly. The cases were consecutive ones, that is to say so long as the post-mortem examination had been secured no selection of cases has been made; if they had hyperpiesis and died, and a post-mortem was allowed, they were included in the series. In a considerable number of the cases one kidney was removed before autolysis could have occurred, and was at once injected through the renal artery with a mixture of equal parts of Müller's fluid and 10 per cent. formalin solution. The post-mortem observations were carried out by the Pathologists of the Hospital, and the microscopic examination of one kidney or both kidneys of each case was directed (1) towards the condition of the Malpighian corpuscles; (2) to the condition of the tubules; (3) to the condition of the arterioles of the kidney; and (4) to the presence or absence of fibrosis.

CASE 1.—J. W., domestic servant, æt. 26, ward 7, bed 15. Register No. 1061. Admitted April 21, 1907. Died April 24, 1907. P.M. Register No. 82.

Symptoms.—The patient was admitted to hospital for loss of consciousness and had a fit in the cab on the way to the hospital. For three or four years she had been ill on and off, with vomiting, shortness of breath and general weakness. She had had hæmatemesis on several occasions, the last time on April 19, 1907. There had been also epistaxis, and occasionally the face had been puffy. She had frequently during these years had to give up work for short occasions, owing to weakness. She was liable to excessive thirst and nycturia was a feature two to three times in a night. She had formerly had typhoid fever, but no other illness. A year prior to admission to the hospital she was in the service of a doctor, who, finding that she was occasionally "faint," examined her, but could detect nothing wrong with her heart; no further examination was made by him.

Physical Signs.—The patient lay comatose in bed, and slight twitching was seen of the face, arms and legs. She came round and complained a little of thirst. Whilst in the ward she passed but little water. There was no dropsy of the body or limbs. Two examinations were made of the water, and albumen found on both occasions. Hyaline, epithelial and granular casts were also found. The brachial arteries were not

tortuous. The maximum impulse of the heart was in the fifth space internal to the nipple line, it was forcible, and a systolic murmur was heard over the sternum on the level of the second rib. The report on the fundi was as follows: "Both fundi healthy, no neuritis or retinitis, and retinal arteries do not show any degenerative changes." A repetition of fits occurred on April 24, after which she became unconscious and shortly afterwards died. The temperature during her short stay in the hospital varied from 100° to 97°·2.

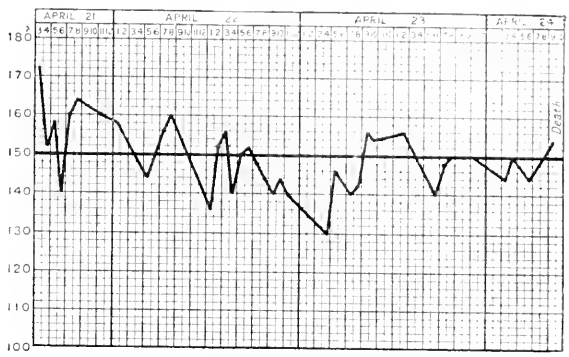


CHART 1.

P.M. Report.—The heart weighs 13 oz.: hypertrophy of the chamber walls is general: no obvious change in the muscle, either naked-eye or microscopically: each kidney weighs 2½ oz., shows a raspberry-like surface on stripping off the capsule, and is very tough on pressure: the cortex is reduced.

P.M. Diagnosis.—Granular Kidney.

Microscopical Examination.—(Kidney injected.[1])

Summary.—Moderate arterio-sclerosis of the larger arteries. Hyaline disease of the glomerular capillaries and afferent arterioles. Marked tubular atrophy.

Details.—The capsule of the kidney is thick. Almost all the Malpighian corpuscles are destroyed: a few are still functional, in some of these the capsular epithelium is swollen, and in a few proliferated: destruction of the corpuscles appears to have resulted from necrosis of the tuft, in some cases with, in some without hyaline change: the glomerular capsules are only slightly thickened: in a few of the corpuscles there are evidences of a previous capsulitis. The cortex measures 3 mm. in width, and contains a thick network of atrophic tubules with fibrosis: the tubules are partly of the simple atrophic variety, partly the shrunken tubules of chronic parenchymatous nephritis: the intervening islands of functional and dilated tubules contain granular material and blood casts. Lymphocytes are abundant in cortex and medulla. The arteriæ arciformes show considerable thickening of their walls and the relation of intima to intima and media (I : I+M = 2 : 6),[2] with slight intimal sclerosis, which may be apparent and due to "crinkling": these changes are slighter in the inter-lobular arteries, but many of the afferent arteries show marked hyaline thickening, with narrowing of the lumina.

CASE 2.—E. W., housewife, æt. 41, ward 7, bed 4. Admitted April 4, 1907. Discharged May 17, 1907. Register No. 905. Second admission ward 14, bed 14. Re-admitted August 30, 1907. Died November 9, 1907. Register No. 2088. P.M. Register No. 204.

[1] The reader will observe that reference is made in the microscopical examination of each kidney to "injection." The injection used consisted of equal parts of 10 per cent. formalin and Müller's Bichromate of Potash solution. The fluid was injected into the kidney through the renal artery within a few hours of death. Where such injection has been carried out, the microscopic changes described in the parenchyma of the kidney may be taken to represent much more the actual ante-mortem condition than if post-mortem autolytic changes had been allowed to occur.

[2] Mr. Lawrence has adopted this plan of expressing the proportionate width of the intima to the intima and media and has made reference to the presence of "crinkling" of the media, so as to provide the reader with some idea as to whether the intimal thickening is merely artifact and due to the presence of contraction of the media or not. If "crinkling" of the intima is present, then some of the thickening of the media is due to the contraction of the muscular coat of the artery; if absent, then the thickening of the media is due to increase of the elements of the middle coat—arterio-sclerosis. The same phenomena of "crinkling" will help the reader to appreciate whether or not this increase of the intima is due to "crinkling" or to intimal proliferation (endarteritis).

Symptoms.—The patient was admitted with dropsy and ascites, shortness of breath and palpitation. The shortness of breath was the first symptom she had complained of, and dated from two years previous to admission. She had had scarlet fever at 6 years of age.

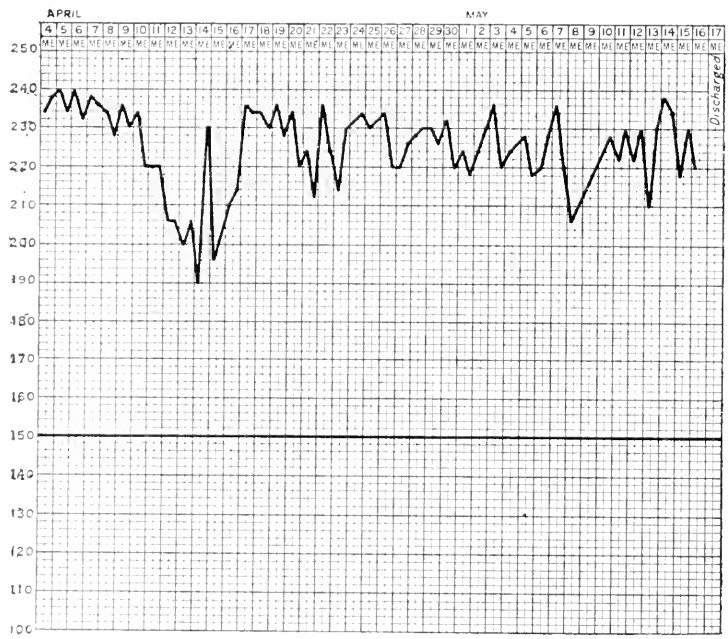


CHART 2A.

Physical Signs.—The patient was of high-coloured complexion. The brachial artery was tortuous. The M.I. was forcible, felt in the fifth space about $4\frac{1}{2}$ inches from the middle line, external to the nipple line: a low-pitched systolic murmur was heard at the apex, both second sounds at the base accentuated. There was well-marked albuminuric retinitis and also some papillitis, especially of the left eye; the veins were engorged. There was œdema.

CHART 2B.

On the first visit to the hospital albuminuria was found twenty times, and the urine was free from albumen four times. On the second visit to the hospital albuminuria was present fifteen times, and absent once. Fever was present occasionally during both periods of stay in the hospital. Death was sudden and unexpected.

P.M. Report.—The body, which is dropsical, is found to weigh 10 st.: the heart weight is 23 oz.: both ventricles are dilated and their walls hypertrophied, the mitral valve is thickened. The kidney weights are 7 and $7\frac{1}{2}$ oz.: both kidneys are large, the capsules adherent, leaving a slightly granular surface: the kidneys are reddish-brown in colour, the cortex is enlarged and tough, the Malpighian corpuscles are not distinct, the pyramids are slightly congested. The renal arteries and arterioles are thickened.

P.M. Diagnosis.—Chronic Bright's Disease: Mitral Regurgitation.

Microscopical Examination.—(Kidney not injected.)

Summary.—Slight arterio-sclerosis: slight glomerulo-tubular atrophy, due probably to a past capsulitis.

Details.—Capsule of kidney absent. About 10 per cent. of the Malpighian corpuscles are destroyed; the tufts are either necrotic or compressed and atrophic without total destruction of nuclei: 90 per cent. are functional, but many of them show slight hyaline change in the capillaries and hyaline thickening of the fibrous capsule: in a few there is slight proliferation of the capsular epithelium (in six). There are medium-sized areas of tubular atrophy with fibrosis, scattered through the cortex: the remaining tubules show swellings and granular destruction of the epithelium: the cortex measures 6 mm.: lymphocytes are very few.

The arteriæ arciformes are very slightly thickened, the increase being due to intimal sclerosis and not to "crinkling." (I : I+M = 1 : 3): the interlobular arteries show a similar change.

Case 3.—J. W., fishmonger (afterwards a cab-driver), æt. 40, ward 8, bed 3. First admission November 24, 1905. Discharged December 7, 1905. Register No. 2436.

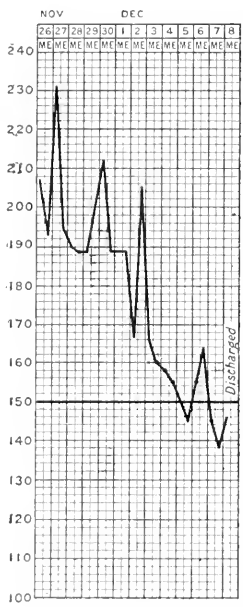


Chart 3A.

First Admission.—Symptoms.—The patient was admitted for shortness of breath for twelve months. A fortnight prior to admission both legs began to swell as well as the lower part of the body: he also began at that time to feel giddy and have headache. There was a history that he drank 7 to 8 pints of beer a day. He had had gonorrhœa, and his wife had had one miscarriage.

Physical Signs.—The patient was a strongly built man. The chest was emphysematous, the left border of the heart was just internal to the nipple line, judged by percussion: the maximum impulse could not be felt: the aortic second sound was very accentuated, no murmurs heard. The brachial arteries were tortuous. In a few days the generalised dropsy began to clear up, the headaches disappeared somewhat. The funduses of the eyes revealed no abnormality. There was a little fever, 99° to 100°·2 during his stay in the hospital. There were five examinations of the urine, and albumen was found on every occasion, a large quantity being present, amounting on two occasions to 3 and 3·5 per mille (Esbach). There was no report on the presence or absence of casts. The patient was discharged improved.

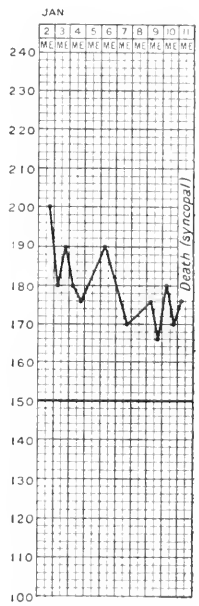


Chart 3B.

Second Admission.—The second admission to the hospital took place on January 2, 1908, and death took place on January 11, 1908, at the age of 42. Ward 8, bed 4. Register No. 11. P.M. Register No. 10.

Symptoms.—On this occasion the patient was affected with severe headaches, shortness of breath and vomiting when he took even the smallest amount of food: general weakness in the legs was noticed: all these symptoms had begun about three weeks previously. For the rest of the period of over two years since his first admission he had been free from any symptoms.

Physical Signs.—The patient was a well-nourished man: his breath was found to be offensive. The M.I. was not forcible, but was present in the fifth space just external to the nipple line: no murmurs were to be heard, and the second aortic sound was a little accentuated. Emphysema was present. Before death pericardial friction

sounds developed over the heart. Syncopal attacks finally developed, and he died in the third one. The brachial arteries were found to be tortuous ; albuminuric retinitis was present. Examination of the urine was carried out on four occasions, when a thick cloud was always found. There was no report of casts being found. Fever was present for four days, the maximum being 99°·4. There was some dropsy.

P.M. Report.—The body weighs 9 st., is well nourished and there is no œdema of the body, but of both legs. The heart weighs 17 oz., the left ventricle is hypertrophied, the coronary arteries are atheromatous, the aortic and mitral valves are free from endocarditis : the mitral orifice admits four fingers : there is some dilatation and hypertrophy of the right ventricle : the larger arteries show thickening of the media, the smaller arteries only slight thickening of the media : recent pericarditis is present. The kidneys weigh $4\frac{1}{2}$ oz. each, and are slightly smaller than normal, the capsule strips off easily, leaving a slightly granular surface : there are a few cysts on the surface, the cortex is slightly diminished, is tough and mottled : the arterioles are thickened : streaks of biurate of soda are seen in some of the tubules.

P.M. Diagnosis.—Red Granular Kidneys, Œdema of the Lungs, Pericarditis.

Microscopical Examination.—(Kidney injected.)

Summary.—Marked arterio-sclerosis and hyaline disease of arteries and capillaries. Marked glomerular atrophy, due to hyaline capillary disease. Marked tubular atrophy.

Details.—The capsule of the kidney is thickened. About 70 per cent. of the Malpighian corpuscles are completely destroyed : 30 per cent. partially : the tufts are reduced to hyaline or granular non-nucleated masses, surrounded by the moderately thickened and shrunken capsules. The cortex is 5 mm. in width ; it shows large areas of atrophied tubules, also cloudy swelling, with variable intertubular fibrosis : lymphocytes are rather abundant in places : the functional tubules are somewhat dilated, and contain hyaline casts. The arciform arteries show marked thickening of the middle coat and slight intimal sclerosis, independent of "crinkling" (I : I+M = 4 : 9), the same condition occurs in still greater degree in the smaller arteries, and in places the intimal thickening is extreme, and often markedly hyaline.

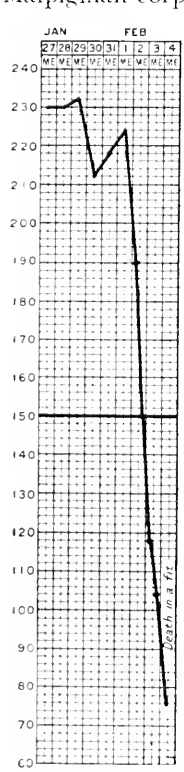


Chart 4.

Case 4.—M. K., housewife, æt. 40, ward 7, bed 21. Admitted January 27, 1908. Died February 4, 1908. Register No. 254. P.M. Register No. 26.

Symptoms.—The patient had had three miscarriages. She was admitted for shortness of breath of two months' duration, and for cough and hæmoptysis for two weeks before admission.

Physical Signs.—The patient sat propped up in bed and had dyspnœa. There was no dropsy. There was headache, vomiting after breakfast, also diarrhœa, and there was a sensation of giddiness and faintness on standing. She looked older than her years, and was rather wasted. A few fine petechiæ were present on both legs. The brachial artery was tortuous. The M.I. was forcible and could be felt in the fifth and sixth spaces internal and external to the nipple line : the aortic second sound was accentuated. The urine was examined three times and always showed albumen, varying from 0·2 to 0·4 per cent. (Esbach). Casts were looked for, but none found. Albuminuric retinitis was observed. There was extreme anæmia, shown by blood count. Signs of pleurisy and œdema of the lungs developed, the diarrhœa and vomiting persisted up to death in a fit, which was immediately ushered in by some delirium. The temperature was normal throughout her stay in the hospital.

P.M. Report.—The body weight is 5 st. 12 lb., the heart weight 16 oz., one kidney weighs $3\frac{1}{4}$ oz., the other $2\frac{1}{2}$ oz. The heart shows slight pericarditis, hypertrophy of

the left ventricular wall, and slight hypertrophy also of the right ventricular wall. There is broncho-pneumonia and pleurisy in the left lung. The kidneys are small, the surface is finely granular, cysts are present, the capsule strips with difficulty: the cortex is narrowed to less then $\frac{1}{8}$th of an inch in width, is pale and tough: the renal arterioles and the renal arteries show thickening of the middle coat and a little atheroma. The thoracic aorta is elastic and shows very few atheromatous patches: the abdominal aorta shows very marked atheroma: the femoral artery shows marked thickening of the media: the dorsalis pedis is thinner than normal: the mesenteric arteries show slight thickening of the media and atheroma: the splenic artery is dilated and tortuous and atheromatous: the carotid shows thickening of the media, and fatty patches in the intima. The intestines were hyperæmic, but not ulcerated.

P.M. Diagnosis.—Red Granular Kidneys: Broncho-pneumonia, Pleurisy.

Microscopic Examination.—(Kidney injected.)

Summary.—Marked tubular atrophy, the result of severe arterio-sclerosis, mainly of the smaller arteries.

Details.—The capsule of the kidney is thickened. About 7 per cent. of the Malpighian corpuscles are destroyed; in them the tuft is necrotic and shrunken and the capsule shows the unequal thickening characterising a healed capsulitis: the functional corpuscles (93 per cent.) mostly show some hyaline thickening of their fibrous capsules, and some dilatation of the space: proliferation of the epithelium is met with in a few: a slight hyaline thickening of the capillaries occurs in many. Large areas of atrophic tubules are present in the cortex: areas of functional tubules are few and small; the epithelium shows granular destruction and hyaline casts are numerous. Fibrosis is well marked in places, and mostly has a very hyaline character. Lymphocytes are few. The cortex is 4 mm. in width. The arciform arteries show considerable thickening from spasm, with apparent moderate intimal fibrosis, due to "crinkling"; but the smaller arteries show extreme disease, pin-hole lumina, and even obliteration occurring in many.

Case 5.—H. B., cellarman, æt. 39, ward 6, bed 10. Admitted February 10, 1908. Died March 4, 1908. Register No. 399. P.M. Register No. 42.

Symptoms.—The patient was admitted for swelling of the abdomen which began eighteen months previously, also for dropsy which began six months before admission. He had had scarlet fever as a child, and he had been a heavy drinker for eight years prior to admission.

Chart 5.

Physical Signs.—The patient's complexion was pale, he was not short of breath. There was a large umbilical hernia. There was fluid in the peritoneal cavity which was tapped and 14 pints removed: there was also some œdema of the feet. The M.I. was present in the fifth space in the left nipple line, and was forcible: the second sounds at the base were very accentuated and ringing, no murmurs were heard. The brachial arteries were a little tortuous. No report was made on the condition of the retinæ. The urine was examined twice and albumen found on each occasion, and on the second blood was found as well. There was no report on the presence or absence of casts. The liver was found to be a little enlarged. Uræmia developed and was improved temporarily by lumbar puncture. Finally, erysipelas developed and "hissing" breathing and restlessness became marked features just before death. The temperature was raised for the first week whilst he was in the hospital, the maximum being 100°·2, then became normal and subnormal, and rose again during the last three days to a maximum of 102°·2 in the axilla.

P.M. Report.—The body is that of a well-nourished man: there is œdema: the weight is 8 st. 12 lb., 6 pints of fluid are present in the abdominal cavity. The liver is large, weighs 48 oz. and shows pericapsular thickening; its surface is granular and on section shows typical multilobular cirrhosis. The heart weighs 15 oz.: the left ventricle is hypertrophied, all the valves and orifices are normal: there is no pericarditis: the aorta and large arteries show very little thickening: the mesenteric vessels show slight thickening. The kidneys are large, dark, and filled with blood, the right weighing 8 oz., and the left 10½ oz., the surfaces are slightly granular: the capsule of the kidneys is thickened and strips with difficulty: on section the cortex is wide and dark and the substance firm: the renal arteries show only a slight thickening: the small renal arterioles show marked thickening.

P.M. Diagnosis.—Renal Sclerosis: Cirrhosis of the Liver, Ascites and Erysipelas.

Microscopical Examination.—(Kidney injected.)

Summary.—Chronic glomerulo-tubular nephritis, with patches of acute parenchymatous change.

Details.—The Malpighian corpuscles are abundantly nucleated, many of them of large size and markedly lobed. In a considerable number the capsule contains many layers of proliferated epithelium. Only 1 or 2 per cent. completely atrophied glomeruli are to be seen. Almost all of the glomerular capsules show distinct hyaline thickening of the fibrous layer. There is a fairly evenly diffused and moderate increase of fibrous tissue between the tubules: the absolute amount of new tissue, however, varies somewhat in different parts.

Most of the tubules of the cortex are reduced in size, their epithelium small, cloudy and granular; the nuclei closely placed. Width of cortex 7·7 mm. Hyaline casts are scanty.

The vessels are practically normal: no "crinkling" of intima (I : I+M = 1 : 3). There is intense congestion of the cortex and in one or two places blood is present in the tubules and glomerular capsules. Round-celled lymphocytic exudate is scanty: capsule of kidney very slightly thickened.

Case 6.—J. F., painter, æt. 27. Admitted into the hospital in 1891 for symptoms pointing to plumbism, and for œdema and vomiting (June 22 to June 30).

Symptoms.—He was readmitted on July 25, 1891 for severe lead colic, and complained of pain in his stomach and across his forehead, diarrhœa and sickness and pain in his knees. He had been in the Army. The urine was examined on four occasions during the first term of admission, and no albumen was found. On this the second admission (July 1891) albumen was found on two occasions, "a trace" and "a good trace."

The third admission (ward 6, bed 1) was on September 16, 1909. He was discharged October 5, 1909 (Register No. 2279). Three months prior to this third admission he woke up suddenly from sleep with a peculiar feeling over his heart which "thumped violently," and he noticed great breathlessness. This lasted a few minutes, and then he lost consciousness for from five to six hours. A second "attack" followed a few days later, and was heralded by twitching of the left arm, but he did not lose consciousness. Since the beginning of the attacks three months previously he had had about two a week: they lasted for from five to ten minutes. There was no incontinence, no biting of the tongue and no cry. He said that besides the illnesses above referred to in his first and second admissions to the hospital, he had had several lead-colic attacks, and eleven years ago lost consciousness in one of these attacks. He has had repeated attacks of true gout during the last sixteen years.

Physical Signs.—Examination of the right eye showed no hæmorrhage or exudation: the fundus of the left eye showed extreme blurring of the inner edge of the disc and some white patches to its outer side: no hæmorrhages. He was pale, complained of a dull headache, and showed tophi in both ears. The brachial arteries were tortuous. The M.I. was present in the fifth and fourth spaces, dislocated outwards, and was a little "heaving" in character: the aortic second sound was accentuated. There

was fever only on two days, reaching 99° and 100°. The urine was examined eight times, and albumen was always present, a cloud to a faint cloud. Petechiæ were present. He was discharged improved.

Fourth Admission.—The patient was readmitted for the fourth time on December 18, 1909, æt. 42 years. Discharged January 18, 1910. Ward 6, bed 22. Register No. 3274.

Symptoms.—The patient was readmitted for what he called his "attacks." One came on the day before admission, and was ushered in with headache and dizziness, and twitching of the left side of the body. It was said that he had had four attacks in succession, but he had no recollection of them. Nycturia had been a feature for some time.

Physical Signs.—He was very drowsy and anæmic. Twitching was observable all over the body, but more especially on the left side: it, as well as the drowsiness,

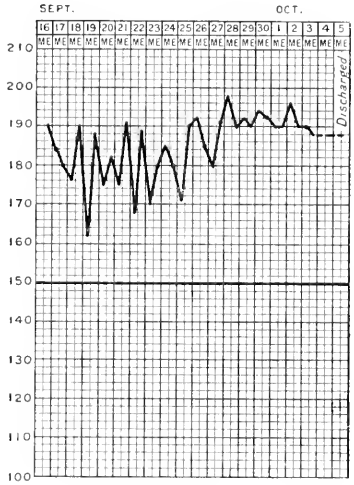


CHART 6A.

CHART 6B.

disappeared shortly after admission. Dyspnœa was marked on the night of admission. The M.I. was felt with difficulty in the fifth space, and was heaving in character: there was so much emphysema that it was difficult to define the area of cardiac dullness: there were no murmurs, but the aortic second sound was accentuated. The lungs were free of abnormal signs, and there was no dropsy. The brachial arteries were tortuous. The supinator and triceps-jerks were more marked on the left side: the abdominal reflexes were diminished at the left side, the plantar response was extensor on the left side, and flexor on the right. The knee-jerks were exaggerated on both sides, but there was no ankle-clonus on the right, and only a suspicion on the left. The right fundus oculi was normal, the left fundus showed a ring of small white spots round the macula, no hæmorrhages, no papillitis, etc.

Eleven days after admission severe headaches occurred, followed by six epileptiform seizures. An attack of gout occurred whilst in the hospital. As the fits were not repeated, he was discharged. The temperature was normal, except a few days prior to the attack of gout, when it reached 102°·2, and on four or five other occasions when it reached about 99°. The urine was examined six times, and the albumen varied from a faint cloud to a cloud. No record of the examination for casts.

Fifth and Last Admission.—Æt. 46. Admitted March 4, 1910, *i.e.* six weeks after last discharge. Died on March 5, 1910. Ward 8, bed 7. Register No. 697. P.M. Register No. 42.

Symptoms.—Since his last discharge from the hospital the patient had been fairly

well until the day of present admission; but had been quite unable to work. Without any warning he had had a fit, the left arm and leg being especially affected, and he became unconscious. He recovered consciousness in half an hour, but soon became unconscious and convulsed again, and the *right arm and leg* were noticed to be more involved in the convulsive movements. He recovered from this second attack, but this was soon followed by another seizure, for which he was admitted, and from which he did not recover. There were rigidity and sometimes twitching in the limbs of both sides of the body.

Physical Signs.—On admission he was deeply comatose, had stertorous breathing, and was cyanosed. The pupils were small, the left rather larger than the right. There was some rigidity in all the limbs. The knee-jerks were present and equal, ankle-clonus and extensor plantar response were present on both sides: the abdominal reflexes were absent. The arteries were found as before to be tortuous, and nothing definite was made out of the heart. Lumbar puncture was carried out, and about 1½ oz. of blood-stained cerebro-spinal fluid was withdrawn. Subsequently venesection was performed, but neither operation led to a return of consciousness, and he died. There was no report on the examination of the urine. The blood-pressure was 245 mm. before venesection, and 204 mm. afterwards.

P.M. Report.—The body is that of a well-built, muscular man: it is free from œdema and cyanosis, and weighs 7 st. 1 lb. The brain reveals some blood in the meninges on the left side along the Sylvian fissure: there is a large hæmorrhage into the brain on the left side extending from the posterior part of the Island of Reil nearly as far back as the end of the posterior horn of the lateral ventricle: it has perforated into the lateral ventricle: the vessels of the brain are dilated and thickened. The heart weighs 16 oz., the left ventricle is hypertrophied, the valves and orifices are normal: the coronary arteries are dilated and atheromatous: numerous atheromatous patches are present in the aorta, some of which are calcified: the mesenteric vessels are not thickened: the brachial artery is thin and dilated, the radial artery is normal. The kidneys, weighing 4 oz. each, are small, there are numerous large cysts, the contents of some are viscid: the capsule is adherent, the kidney is red and finely granular: the substance is tough, and the cortex narrow. Biurate of soda is visible within the tubules.

P.M. Diagnosis.—Red Granular Kidneys, left Cerebral Hæmorrhage.

Microscopical Examination.—(Kidney not injected.)

Summary.—Chronic glomerulo-tubular nephritis.

Details.—The capsule of the kidney is normal. Almost all the Malpighian corpuscles are diseased, though very few are actually destroyed. Many show marked proliferation of the capsular epithelium: in some the capsule is dilated, in others there is partial or complete obliteration, with thickening of the fibrous layer. Slight hyaline change is present in many of the tufts. The cortex measures 6·5 mm., its tubules are small and shrunken, showing finely granular cytoplasm: some are dilated and show hyaline casts. Blood is present in some of the tubules of the medulla. Fibrosis is well marked and fairly diffuse. Lymphocytes are scanty and diffuse, with definite collections in places.

The arteries are normal, except for slight sclerosis in places (I : I+M = 0·5 : 2·5).

Case 7.—E. M., house-parlourmaid, æt. 43, ward 7, bed 15. First admission December 9, 1907. Discharged January 31, 1908. Register No. 3200.

Symptoms.—The patient was admitted for headaches which she had had as long as she could remember: they were worse after work. She also had pain in her eyes which came on suddenly five years previously, and persisted even in recumbency. She had had morning sickness for the last three weeks, and had also had shortness of breath on going upstairs. The katamenia did not begin until the age of 23. Five or six years ago she attended the Moorfields Hospital for defective sight, and was told that her eyes were "very bad." She had had to get up at night to pass water two or three times for the last two years.

CHART 7A.

Physical Signs.—The patient was a thin woman of yellowish complexion. The M.I. was in the fifth space in the left nipple line, and forcible, and there was a systolic murmur at the apex of the heart (? exocardial): the aortic second sound was loud and ringing, and there was a systolic murmur at the pulmonary cartilage (? exocardial). The brachial arteries were tortuous. Report on funduses: "There is a considerable swelling of the right disc, and retinitis, with much exudation. The exudation forms a star-shape figure at the macula, and is interspersed with hæmorrhages in the nerve-fibre layer. In the left eye the same condition of the disc is present, the exudation in the retina is considerable, several patches are seen round the disc and several small bright patches at and below the macula, not forming a definite star figure. There are numerous hæmorrhages in the nerve-fibre layer." Twenty-two examinations of the urine were made, and albumen always found, varying from one-third to a mere cloud: a few hyaline and granular casts were found. The temperature was subnormal throughout her stay, except for a few days when it reached 99°. Vomiting was a feature of her illness. Eventually she was so much improved that she was discharged.

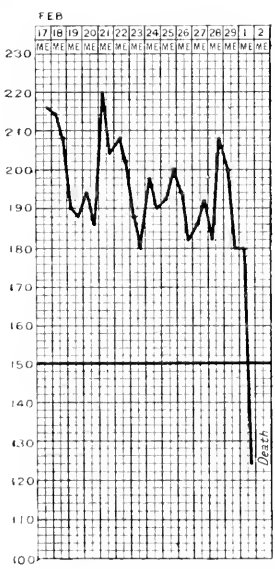


CHART 7B.

Second Admission.—She was admitted for a second time on February 17, 1908, to ward 7, bed 23, and died on March 1, 1908. Register No. 465. P.M. Register No. 37.

Symptoms.—The patient had only been out of the hospital seventeen days when she was obliged to seek re-admission on account of the return of her symptoms.

Physical Signs.—The patient looked ill on admission, and was very much wasted but free from dropsy. She had an herpetic eruption on the left side of the chest. The physical signs were the same as those above reported. The patient became drowsy, and slight twitching was seen in the thumbs: her wasting continued, her breath became sighing in character, but not periodic. Purpuric spots developed on the abdomen. The drowsiness increased, and she became unconscious and died. It was noticed that the M.I. was still forcible, and was external to the nipple line. There were eight examinations of the urine, and albumen was found on each occasion. The temperature on this occasion was subnormal or normal. The funduses of the eye still showed marked retinal changes.

P.M. Report.—The body is poorly nourished, and weighs 8 st. 3 lb. There is marked pericarditis, the left ventricle is hypertrophied, the mitral and aortic valves are normal, the coronary arteries are normal, the right ventricle is dilated and hypertrophied, the tricuspid valve is normal: the heart weighs 14 oz. Both kidneys are small, weighing 2½ oz. each, they are pale, there are numerous cysts on the surface, the capsule is thickened and strips with difficulty, the surface is markedly granular: the cortex is pale, but not very much diminished: the renal arterioles are thickened, also the main renal arteries. The aorta is slightly atheromatous, the mesenteric arteries are not thickened. Patches of broncho-pneumonia are found in the lungs.

P.M. Diagnosis.—Red Granular Kidney, Pericarditis, Broncho-pneumonia.

Microscopical Examination.—(Kidney injected.)

Summary.—Marked glomerular destruction, probably from healed capsulitis. Marked tubular atrophy. Marked arterio-sclerosis.

Details.—The capsule of the kidney is thick. About 34 per cent. of the Malpighian corpuscles are destroyed, probably as the result of capsulitis; 66 per cent. are functional: the capsules are mostly dilated, and there is slight hyaline thickening of the capillary tufts and fibrous layer of the capsules. The cortex is 3 mm. in width, or less. Large tracts of atrophic tubules with intertubular fibrosis occur, the intervening islands having the tubules much dilated, so as almost to constitute cysts and containing hyaline casts in abundance. Lymphocytes are present in patches. The arciform arteries are much thickened and not in spasm, and there is a moderate intimal sclerosis not due to "crinkling" (I : I+M = 2 : 6). The sclerosis is more marked in the smaller arteries, and in some there appears to be complete occlusion, with or without thrombosis.

Post-mortem estimation of the error in the sphygmomanometer reading, attributable to stiffness of the vessels, showed that the latter might amount to 16 mm. Rigor mortis had already set in; but probably this would not seriously have affected the result, because rather than increase the figure 16, it would have diminished it.

Case 8.—C. C., wood-carver, æt. 45, ward 8, bed 19. Admitted November 29, 1907. Died March 18, 1908. Register No. 3102. P.M. Register No. 55.

Symptoms.—The patient was admitted for shortness of breath and swelling of the body, dating from three or four weeks previously. Eleven months prior to admission he had been said to have Bright's disease. Six months before admission there had been much rectal bleeding, owing it was said to piles. Some defect in his sight had been noticed for six months, and this had intensified.

Physical Signs.—The patient sat propped up in bed, and looked very ill. The eyelids were puffy, and there was dropsy of the trunk and of all four limbs. Fine crepitations were heard over the bases of both lungs. The M.I. was found in the fifth space, 1½ inches external to the nipple line: it was heaving in character, and was accompanied by a soft murmur: the second aortic sound was accentuated. Friction sounds were heard in front of the heart on December 5, 1907. The brachial arteries were tortuous. The urine was examined forty-five times, and albumen was found as a faint cloud or trace on thirty-seven occasions: it was absent on eight occasions: the urine contained a few granular and fatty casts. During his stay in the hospital the temperature, with the exception of two or three days, was subnormal. The eyes showed diffuse albuminuric retinitis. Purpuric spots ultimately developed on January 3, 1908, after drainage of the limbs had been carried out on several occasions. Six days before death he had a fit and lost consciousness, and before death the fits were repeated thirty times. Cheyne-Stokes breathing also developed, and he died shortly after the last fit. The observations on the blood-pressure, begun some time after admission, are open to criticism, as there was some œdema of the arms, and he had to be propped up in bed.

P.M. Report.—Body weight 8 st. 10 lb. Œdema of the body and limbs is present, and a great excess of fluid in all serous cavities. Lymph is found on the pericardium: the left ventricle is greatly hypertrophied: the mitral and aortic valves are free from endocarditis, but the mitral orifice admits five fingers: there is some hypertrophy of

the right ventricle : the heart weighs 22 oz. The kidneys weigh 3 oz. each, they are small, pale and finely granular, numerous cysts are present, the capsule is thickened and the cortex is reduced to $\frac{1}{16}$th of an inch ; the cortex is pale, the pyramids are red, the renal arteries and arterioles are thickened. The aorta is slightly thickened, the mesenteric vessels are thickened, and there is marked atheroma in the vessels of the legs. At the junction of the sigmoid with the rectum there is a mass of carcinomatous growth 1 inch in diameter. Secondary deposits are found in the liver and lung.

P.M. Diagnosis.—Granular Kidneys, Carcinoma of the Sigmoid Flexure, Secondary Deposits in the Lung and Liver. Pericarditis.

Microscopical Examination.—(Kidney injected.)

Summary.—Marked arterio-sclerosis. Marked glomerular atrophy, the result partly of a healed capsulitis, partly of hyaline capillary disease. Marked tubular atrophy.

Details.—The capsule of the kidney is thick. About 50 per cent. of the Malpighian corpuscles are destroyed : most of these show signs of an old capsulitis, but many show what appears to be a simple anæmic necrosis of the tuft, in some cases combined with hyaline thickening of the capillaries. The functional corpuscles almost all show some

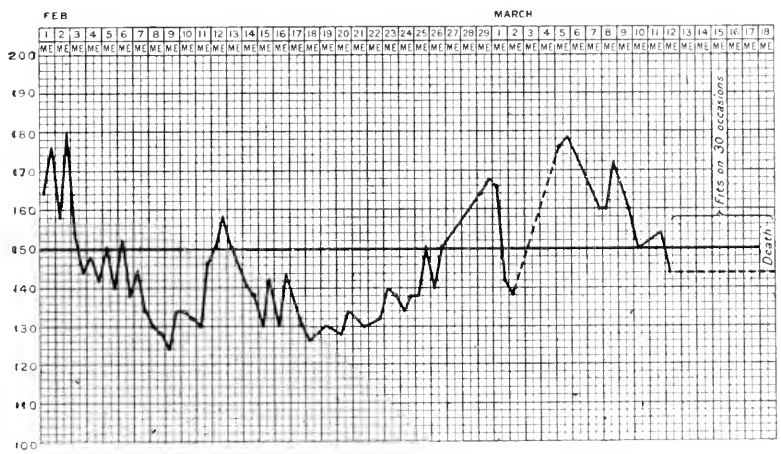


CHART 8.

compression of the tuft, and thickening of the fibrous layer of the capsule, and many show some hyaline thickening of the capillaries ; in one or two there is slight proliferation of the capsular epithelium. The cortex measures 3 to 5 mm. in width : it shows large areas of atrophic tubules, with islands of functional tubules, which are dilated and contain epithelium undergoing granular breakdown. Fibrosis is in general slight, but fairly marked in some spots. Lymphocytes are present in places. The arciform arteries show marked thickening independent of spasm (I : I+M = 4 : 7), and intimal sclerosis not due to " crinkling " ; the change is still more marked in the smaller arteries, many of which have pin-hole lumina.

CASE 9.—J. W., stoker, æt. 75, ward 6, bed 18. Admitted May 1, 1908. Died May 24, 1908. Register No. 1169. P.M. Register No. 96.

Symptoms.—The patient was admitted for shortness of breath, pain in the legs and at the back of the head of three weeks' duration. The only antecedent illness was scarlet fever.

Physical Signs.—The patient sat propped up in bed, he was free from œdema, but was a little delirious. As a rule his temperature was subnormal, but for a day or two above normal. The M.I. was seen in the sixth space in the left nipple line, it

was not forcible: the second aortic and pulmonary sounds were accentuated, there were no murmurs. There was impairment of the percussion note of the lower part of the left chest, over the same area the breath sounds were weak, and ultimately an empyema was discovered there, from which he died. There were nine examinations of the urine, and albumen was always found present either as a slight trace, or as a thick cloud. There was no report on the presence or absence of casts, on the condition of the retinæ or of the brachial arteries.

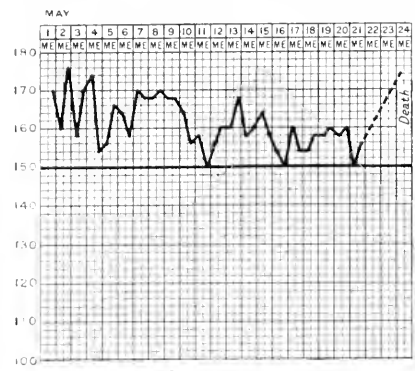


CHART 9.

P.M. Report.—The body weight is 8 st. 7 lb. The left ventricle is hypertrophied, and there are signs of pericarditis: the aortic and mitral valves are normal: the heart weighs 18 oz. The mesenteric arteries are uniformly markedly thickened. The right kidney weighs 5½ oz.; it is large and pale, the capsule strips easily, leaving a finely granular surface; the cortex is normal in consistence: the vessels supplying the kidney are not much affected. The left kidney is small, weighing 2 oz., the pelvis is dilated and the kidney substance is in a condition of hydronephrosis: the amount of renal tissue is much diminished. The lower lobes of the lungs contain recent red infarcts. There is a left-sided empyema.

P.M. Diagnosis.—Hydronephrosis (left), Granular Kidney (right), Pericarditis, Empyema and Infarction of the Lungs.

Microscopical Examination.—(Right kidney injected.)

Summary.—Slight glomerulo-tubular atrophy, probably due to healed capsulitis. Slight arterio-sclerosis. Cloudy swelling of tubular epithelium.

Details.—The capsule of the kidney is very slightly thickened. About 15 per cent. of the Malpighian corpuscles are destroyed, apparently by a past capsulitis: 85 per cent. are functional and normal, except for slight dilatation of the capsule. The cortex measures 5·5 mm. The epithelium of most of the tubules is swollen and cloudy, and in many shows a partial granular disintegration. Small patches of tubular atrophy with fibrosis occur here and there. Lymphocytes are few in number. The arciform arteries are very slightly thickened and free from spasm (I : I+M = 1 : 4), and there is a trifling intimal sclerosis, not apparently due to "crinkling." The smaller vessels are scarcely altered.

CASE 10.—W. P., labourer, formerly a clerk, æt. 52, ward 8, bed 1. Admitted May 4, 1908. Died June 1, 1908. Register No. 1192. P.M. Register No. 102.

Symptoms.—The patient was admitted to hospital complaining of shortness of breath and inability to sleep in recumbency; even walking on the flat caused great breathlessness. He had also noticed that he had lost weight.

Physical Signs.—He was free from dropsy, and had no fever throughout his stay in the hospital. The M.I. of the heart was in the fifth space in the left nipple line, and was heaving in character: no murmurs were heard, some accentuation of the second sounds at the base. The brachial arteries were very tortuous. The urine was examined three times and showed a thick cloud on all occasions: the urine became nearly solid on the first occasion on boiling and adding acetic acid: the specific gravity was 1009, 1011, 1010, the quantity being respectively 45, 51 and 50 oz. The patient's breathing became very difficult on one or two occasions, and he was bled on May 11, 1 pint, and on May 20, 18 oz. Ultimately he died in a comatose condition. There was no report on the retinæ, or on the presence of casts.

P.M. Report.—The body weighs 7 st. 1 lb. The heart weighs 20 oz., the left ventricle is dilated, the mitral orifice is normal, the aortic valves and the aorta show some atheroma. The kidneys each weigh 3½ oz., they are small, the capsule adherent,

the surface granular and pale, the cortex diminished: there is some scarring: the substance is fatty: there are some cysts. Pneumonia present in the lower lobes of the lungs.

P.M. Diagnosis.—Granular Kidney, Lobar Pneumonia.

Microscopical Examination.—(Kidney injected.)

Summary.—Marked glomerulo-tubular atrophy, probably depending upon a healed capsulitis. Moderate arterio-sclerosis.

Details.—The capsule of the kidney is slightly thickened. About 50 per cent. of the Malpighian corpuscles are destroyed; the tuft is shrunken and necrotic, and the capsule adherent and unequally thickened. The functional corpuscles (50 per cent.) are mostly normal, with slightly dilated capsules: in one or two there is slight proliferation of the capsular epithelium. The cortex is 5 to 6 mm. in width: it contains a coarse network of atrophic tubules, with intervening islands of dilated tubules containing granular material. Fibrosis is well marked. Small collections of lymphocytes occur in places.

Both arciform and interlobular arteries show moderate thickening, not due to spasm (I : I+M = 3 : 7), and intimal sclerosis, not due to "crinkling."

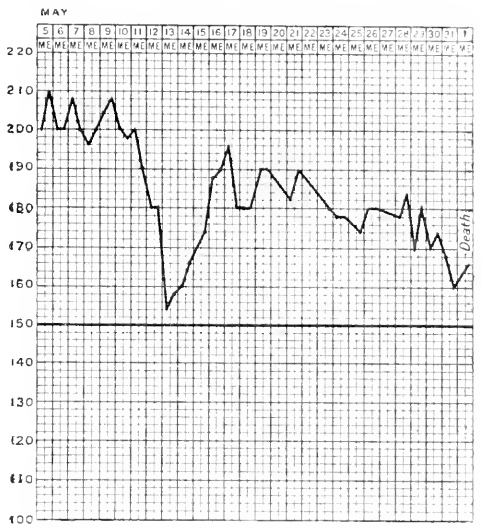


CHART 10.

CASE 11.—T. H., furniture packer, æt. 59. Admitted December 30, 1908. Died January 19, 1909. Ward 8, bed 5. Register No. 3500. P.M. Register No. 10.

Symptoms.—On the day of admission the patient was returning home from work, when on getting off a bus he was seized with severe breathlessness and had to be assisted to the hospital. The fog present on the occasion apparently aggravated his difficulty. During the eighteen months previous to admission he had had three other such attacks of breathlessness, accompanied by headaches. Fifteen years previously he had been operated upon for fistula, and he had also suffered from slight arthritis in the knees and ankles.

Physical Signs—The patient was a stout, fairly healthy-looking man. The lips were a little cyanosed. The chest appeared to be fixed in a position of inspiration, and he could not lie down. There was no dropsy. The temperature for the first fortnight was normal, then rose to as much as 101° during four days, and was about normal just before death.

The brachial arteries were very tortuous. The M.I. could not be felt, the aortic second sound was exaggerated, but the pulmonary second was more accentuated than the aortic. The breath sounds were bronchial in type and a few rhonchi were heard. The funduses of the eyes were normal. The examination of the urine was carried out ten times: on seven occasions there was no albumen, and on three occasions there was a trace or a cloud: hyaline and epithelial casts were found in the urine. The end came about in the following manner: he had gone to sleep on the evening of January 19, then he woke up and vomited, and was seized with violent breathlessness (as severe as when he was admitted) and was convulsed: the pulse rapidly became more feeble, and in ten minutes he was dead.

P.M. Report.—The body is that of a well-nourished man, there is no œdema: it weighs 9 st. 9 lb. The heart weighs 17 oz.: it is free from pericarditis: the left ventricle is enlarged and the wall hypertrophied, and shows some fibroid degeneration of the heart muscle: the aortic valve is competent, the mitral orifice admits three

fingers and appears to be competent, the right ventricle is slightly hypertrophied. The right kidney weighs 3½ oz., the left 4 oz.: they are slightly diminished in size, the surface is granular: no cysts are seen: the capsule is slightly adherent, but does not tear the kidney substance on stripping: the substance of the kidney is tougher than normal, the cortex is slightly diminished, there are streaks of biurate of soda in the tubules: there is no thickening of the renal arteries. The aorta and large vessels are dilated and tortuous, and show numerous atheromatous patches, many of which are calcareous. The coronary arteries show atheroma, the anterior one is practically occluded: the mesenteric vessels contain no atheromatous areas, except one gelatinous patch at the origin of the superior mesenteric artery. The lungs show œdema and bronchitis and old tuberculosis.

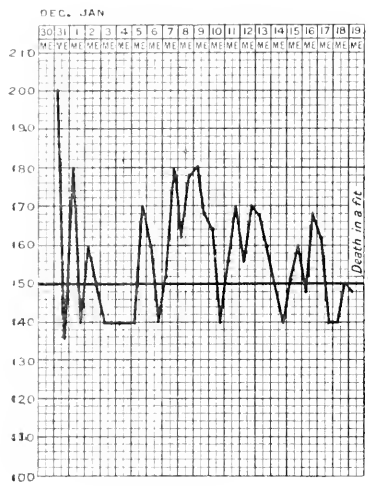


CHART II.

P.M. Diagnosis. — Red Granular Kidneys, Atheroma of the Coronary Arteries, leading to Fibrous Myocarditis, Œdema of the Lungs, Bronchitis and old Tuberculosis of the Lungs.

Microscopical Examination.—(Kidney not injected.)

Summary. — Moderate glomerulo-tubular atrophy, resulting mainly from arterio-sclerosis and hyaline disease, chiefly of the smaller arteries and the capillaries.

Details.—The capsule of the kidney is thickened. About 30 per cent. of the Malpighian corpuscles are destroyed. In the majority of them the change appears to be an atrophy due to hyaline disease of the capillaries, but in some there is evidence of a healed capsulitis. The 70 per cent. functional corpuscles show slight hyaline change in the tuft in many, with slight thickening of the fibrous layer of the capsule. Small areas of tubular atrophy are scattered through the cortex, and slight fibrosis is associated with these. The majority of the tubules show swollen epithelium, undergoing partial granular disintegration. The cortex measures 5·5 mm. in width. Lymphocytes are few in number. The arciform arteries show slight thickening, not due to spasm (I : I+M = 2 : 4), and intimal sclerosis, not due to "crinkling." This is also present in the interlobular arteries, and is very marked in some; but the disease is very unequally distributed.

CASE 12.—T. C., fishmonger, æt. 69. Admitted February 2, 1909. Died February 19, 1909. Ward 6, bed 17. Register No. 319. P.M. Register No. 21.

Symptoms.—The patient was admitted with a history that for eight years he had been troubled with pains in the lower part of the back, coming on at shorter or longer intervals; eight months prior to admission he found he was getting weak and losing flesh, and a fortnight before admission he became very short of breath and his legs became swollen; on admission there was great œdema of the face and body. He noticed that he had to pass water rather frequently. There was a history of excessive consumption of alcohol.

Physical Signs.—The patient was a stout man, and his face looked very puffy. There was general dropsy. The M.I. could not be seen but could be felt in the sixth space three-quarters of an inch external to the left nipple line: no murmurs could be heard, nor was either second sound at the base accentuated. The brachial arteries were tortuous; the chest was emphysematous. There were no symptoms referable to the abdomen, and the only sign was a little depression of the lower margin of the liver. The urine was examined seven times: on the first two occasions there was a faint cloud or a slight cloud of albumen: on the other five occasions there was no albumen at all. There were no observations on casts. The retinæ were examined

and no abnormality found. After admission the dropsy rapidly became much less and gradually disappeared, but he began to be troubled with cough and showed some anæmia.

On February 18, without any special warning, he vomited blood, continuing to do so until he had brought up 68 oz. of blood. He became much collapsed, and his extremities cold and the pulse weak. The hæmatemesis continued, and he became still weaker and died with gradual loss of consciousness. During his stay in the hospital there was never any fever.

P.M. Report.—The body weighs 7 st. 10 lb.; it is well nourished, there is no cyanosis and no dropsy. The heart weighs 18 oz.: the left ventricle is hypertrophied; degeneration is present in the muscle in patches; the valves and orifices of the heart are normal; there is extensive atheroma of the aorta. There is very little thickening or atheroma of the carotid or femoral arteries; the mesenteric vessels show slight thickening. The kidneys weigh 5 oz. each, are slightly increased in size, the surface looks pale, and is slightly granular, the capsule is slightly adherent, and there are a few cysts present: the cortex is a little wider than normal, the small arterioles of the the kidney are normal. The stomach is found to be greatly enlarged, and there is a large mass of growth (carcinoma) occupying the posterior wall. The stomach contains a considerable amount of blood.

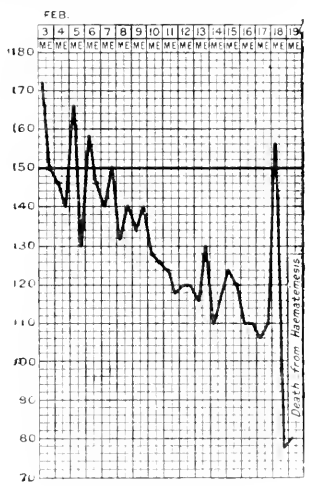


CHART 12.

P.M. Diagnosis.—Early Renal Cirrhosis. Carcinoma Ventriculi.

Microscopical Examination.—(Kidney not injected.)

Summary.—Slight glomerulo-tubular atrophy, probably capsulitic in origin. Slight arterio-sclerosis.

Details.—The capsule of the kidney is slightly thickened. About 15 per cent. of the Malpighian corpuscles are destroyed, in most cases apparently by a healed capsulitis. Eighty-five per cent. are functional and normal, except for some dilatation of the capsules. The cortical tubules are mostly little altered: the lumina are somewhat dilated and contain granular material from partial disintegration of the cells. Small areas of tubular atrophy, with fibrosis, are associated with the atrophied glomeruli. The cortex measures 6·5 mm. Lymphocytes occur in small numbers. There is considerable thickening of the arteriæ arciformes, due to spasm (I : I+M = 2 : 7), with slight intimal sclerosis, apparently in part due to "crinkling." The smaller arteries are scarcely affected.

CASE 13.—B. G., builder's labourer, æt. 54, formerly in the Army. Ward 8, bed 23. Register No. 816. Admitted March 26, 1909. Died April 8, 1909. P.M. Register No. 46.

Symptoms.—The patient was admitted for pain in the right chest and cough for four months; the phlegm was scanty and white. Inability to swallow easily was noticed four days after admission. The pain was increased by breathing. The patient had lost 4 st. in weight in the last four months.

Physical Signs.—Visible pulsation of the arteries of the neck. The M.I. was present in the fifth space in the left nipple line and was feeble and diffuse; no murmurs were heard anywhere: the second aortic sound was accentuated and the brachial vessels were tortuous. There was slight œdema of both legs. The urine was examined five times, and on no occasion was albumen found. There was no report of the presence or absence of casts, nor of the examination of the retinæ. The dullness in the right chest was found to be due to an empyema, and the pus drawn off was highly offensive. Fever was present throughout his stay in the hospital. A reddish area in the wall of

the œsophagus was detected by œsophagoscopy, presenting a granular aspect of a carcinomatous character. Death from starvation and septicæmia.

P.M. Report.—The body weighs 8 st. 9 lb., the heart weighs 13 oz., each kidney weighs 6 oz. The heart is hypertrophied: no abnormality of mitral or aortic valves reported. The kidneys are granular and red, and scarred in places, the capsule strips fairly easily: the cortex is slightly diminished and tough: the renal artery is normal. The œsophagus shows a carcinomatous growth at the junction of the lower and middle thirds, which is ulcerated, and there are peritoneal developments of secondary growths. Empyema in the left pleural cavity.

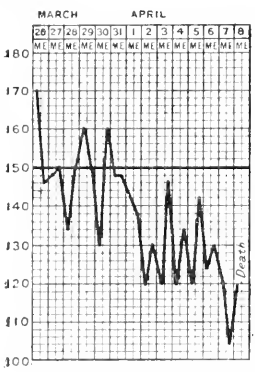


Chart 13.

P.M Diagnosis.—Carcinoma of the Œsophagus, Secondary Glands in the Peritoneum, invading the Stomach and Liver. Red Granular Kidney and Empyema.

Microscopical Examination.—(Kidney not injected.)

Summary.—Very slight arterio-sclerosis: slight glomerular destruction and tubular atrophy: cloudy swelling of renal epithelium.

The glomerular destruction is due to a past capsulitis and independent of the arterial disease. The tubular atrophy is due to the glomerular destruction.

Details.—The cortex measures 4·5 mm., and the capsule of the kidney is slightly thickened. About 7 per cent. of the Malpighian corpuscles are destroyed, and greatly reduced in size: the tuft is devoid of nuclei and no lumina are visible: the fibrous capsule, which adheres to the tuft, shows in most cases a semilunar thickening at one part. Related to these atrophic corpuscles are small areas of tubular atrophy in which a slight amount of fibrosis is present. About 93 per cent. of the Malpighian corpuscles are normal, one or two only showing cloudy swelling of the epithelium. Their related tubules are either dilated, as in the superficial layers of the cortex, or their epithelium is swollen and cloudy, as in the deeper layers.

The arteries are very little altered and are free from spasm (I : I+M = 1 : 2); the arciform arteries show a trifling subendothelial fibrosis, independent of "crinkling," but otherwise their wall is not thickened. Lymphocytic exudate is practically absent.

Case 14.—F. A., housewife, æt. 32, ward 7, bed 2. Register No. 236. Admitted January 25, 1909. Died April 15, 1909. P.M. Register No. 48.

Symptoms.—This patient had had headaches ever since the age of 16 years, which became worse and were accompanied by vomiting during the four and a half months previous to admission. Her sight had been failing for three weeks before admission: occasionally she saw double, and even polyopia had occurred. She had had three miscarriages.

Physical Signs.—On admission she was found to be a well-nourished woman. The M.I. was not forcible, but was displaced outwards, and the aortic second sound was exaggerated: there were no murmurs. The brachial arteries though not visible could be felt to be tortuous. Twenty examinations of the urine were carried out, and the urine showed albumen on every occasion, varying from $\frac{1}{10}$th to $\frac{2}{3}$rds: sometimes there was blood present: a few granular casts were found. There was optic neuritis and retinitis in both eyes, and ultimately numerous retinal hæmorrhages occurred. During her long stay in the hospital the patient was frequently in a semi-comatose condition, and eventually the urine was suppressed, friction signs were heard over the cardiac area, and brownish mottled patches appeared on the backs of the hands. The temperature on a few occasions rose to 99°, but mostly was normal, or subnormal. There was no dropsy. She died comatose.

P.M. Report.—The body weight is 7 st. 2 lb. 8 oz.: the heart weighs $17\frac{1}{4}$ oz.: the right ventricle is slightly hypertrophied, the left ventricle hypertrophied and dilated. There is atheroma of the coronary arteries almost occluding their lumen, and there

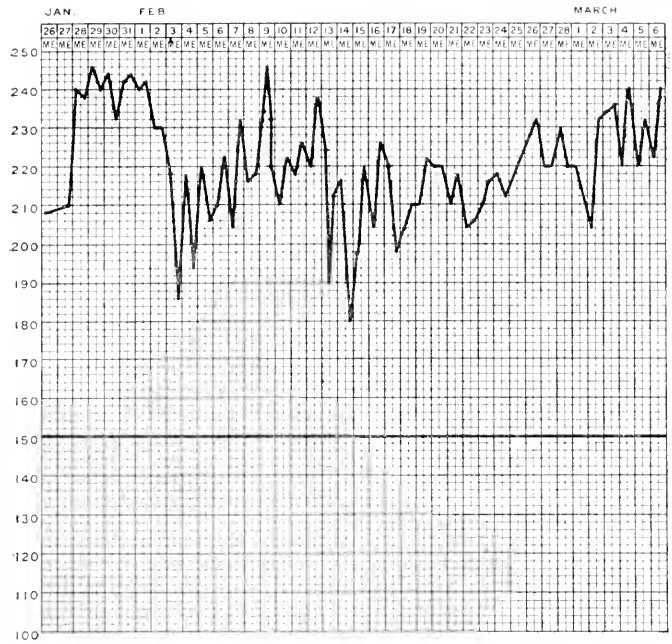


CHART 14.

are signs of recent pericarditis. There is a recent vegetation on the mitral valve which admits three fingers. The arteries of the mesentery show no obvious change. The kidneys weigh $6\frac{1}{4}$ oz. each and are somewhat enlarged, the capsule is thickened and strips off leaving a coarsely granular surface in which there are numerous small hæmorrhages: the kidney substance is pale, there are patches of atrophied cortex in places, in others the cortex is increased: the cortex is also tougher than normal. The condition of the brachial arteries is not reported.

P.M. Diagnosis.—Fibroid Kidneys, Uræmia, Bronchitis and Endo- and Pericarditis.

Microscopical Examination.—(Kidney injected.)

Summary.—Marked arterio-sclerosis and hyaline change, especially of the smaller arteries. Considerable glomerular destruction. Extensive tubular atrophy. The arterial disease is probably the fundamental lesion, and the tubular atrophy is mainly secondary to it. The glomerular destruction appears to have resulted from an independent or superadded capsulitis, and is also probably responsible for a considerable part of the tubular atrophy.

Details.—The capsule of the kidney is thickened. About 30 per cent. of the Malpighian corpuscles are destroyed. The latter are greatly reduced in size and consist of the necrotic tuft surrounded by the capsule, which is mostly thickened in the unequal fashion that results from a past capsulitis. Seventy per cent. of the corpuscles appear to be functional, their nuclei are retained; but many are

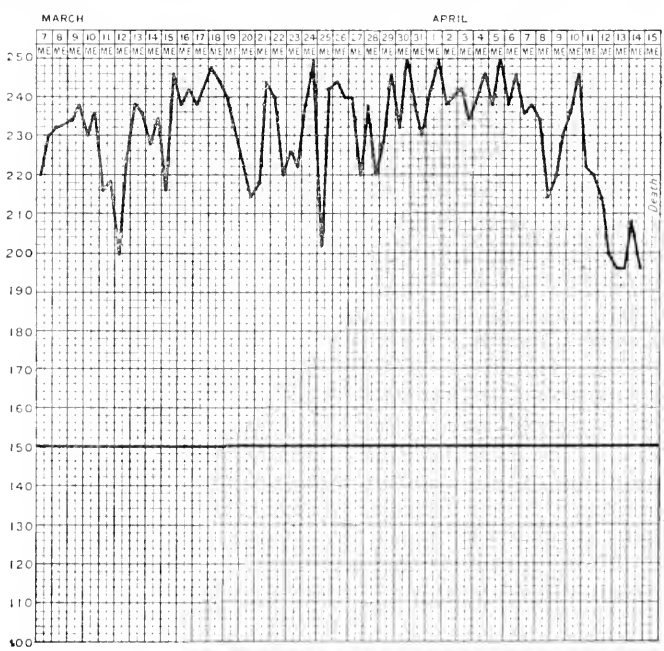


CHART 14 (continued).

small, round, and as if somewhat compressed, and their fibrous capsules are thickened: these and the corpuscles which are still less altered show in many instances some hyaline change in the capillaries: the capsular epithelium is normal, the capsular spaces slightly dilated and free from exudate.

The cortex measures 5 mm. and shows large areas of atrophied tubules, with well-marked fibrosis in many places: the tubules of the intervening areas are greatly distended with colloid material. Considerable collections of lymphocytes are present in places.

The arciform arteries are thickened, independent of spasm (I : I+M = 1 : 6); the thickening is only to a moderate extent due to subendothelial deposit. In the interlobular arteries the sclerosis and narrowing of the lumina are extreme.

Case 15.—R. D., painter during the last nine years, æt. 29, ward 6, bed 6. Admitted to the hospital April 15, 1909. Died on April 30, 1909. Register No. 962. P.M. Register No. 56.

Symptoms.—The patient was admitted with pain in the abdomen and weakness. For fifteen months previously he had been subject to attacks in which he was very sick: his eyelids were "puffy and swollen." Six weeks previous to admission he seems to have had an attack of colic, and a week later cramps in the legs and arms lasting about five minutes on each occasion. During the fortnight previous to admission he had had a cough, and the phlegm was streaked with blood.

Physical Signs.—He showed great pallor, and very slight œdema in the legs. He was conscious; the eyelids were slightly puffy, and the breath was offensive. During his stay in the hospital he was free from fever except on one occasion of twenty-four hours when it reached 99°. The M.I. was in the sixth space in the nipple line, and later external to this position: the aortic second sound was accentuated. The artery at the wrist could be felt between the heart-beats. Two small patches of exudate and papillitis were found in the left fundus oculi. Pericardial friction sounds were heard eight days before death: just prior to death vomiting became a marked feature, twitching movements developed in the arms, and there was retention (? suppression) of urine. The patient died quietly. Four examinations of the urine were reported, and albumen was always present in a fair amount. Casts were looked for once, but not found.

P.M. Report.—The body weighs 9 st. 5 lb., the heart weighs 19 oz., the right kidney 2 oz., the left 3 oz. The body is well nourished; there is some œdema of the legs and feet. The heart shows recent pericarditis: the left ventricular wall is hypertrophied: the right ventricle is slightly dilated and the wall hypertrophied: the coronary arteries show marked atheroma. The mesenteric vessels show slight thickening of the middle coat; carotid, femoral and radial arteries are normal. The kidneys are small and pale, the capsule strips with difficulty, the surface is mottled, is irregular and there are large areas of atrophy of the cortical substance: the cut surface is mottled, and there is some ecchymosis in the cortex: the cortex is markedly diminished in some places; in other places it is wide: streaks of biurate of soda are visible in the pyramids; there is slight thickening of the renal capillaries; the renal arteries show very little thickening. There is pneumonia in the right lower lobe, 1½ pints of thin pus in the right pleural cavity, and the pleura is covered with recent lymph.

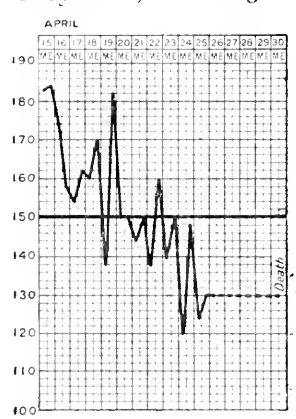


Chart 15.

P.M. Diagnosis.—Chronic Bright's Disease, Pneumonia, Empyema and Pericarditis.

Microscopical Examination.—(Kidney not injected.)

Summary.—Marked glomerulo-tubular atrophy, due to arterio-capillary disease. A slighter degree of glomerular atrophy probably from healed capsulitis.

Details.—The capsule of the kidney is thickened. The disease varies in intensity in different parts, in some (*A*) being moderate, in others (*B*) severe.

A. About 30 per cent. of the Malpighian corpuscles are destroyed, the capsule being shrunken round the necrotic tuft which, in many cases, shows hyaline changes. About 70 per cent. of the corpuscles are functional, but many of them are distinctly diseased. In most the epithelium of the capsule is swollen, in some it is slightly proliferated. In some the capsules are fairly adherent and thickened; in many there is hyaline change in the tufts. The cortex varies in thickness, and in places reaches as much as 8 mm. It contains a coarse network of shrunken tubules, with an irregularly distributed fibrosis. Many of these tubules are simply atrophic, but as many show the irregular form and cloudy protoplasm of Chronic Parenchymatous Nephritis. Scattered hyaline casts are present, and lymphocytes are abundant in places. The arciform arteries show moderate and well-marked thickening, due to spasm or proliferation (I : I+M = 2 : 7), and intimal sclerosis, apparently in part due to "crinkling." The same changes with the addition of hyaline degeneration are present in the smaller vessels, and are here more marked.

B. Almost all the Malpighian corpuscles are destroyed, and are similar in appearance to those in other parts of the kidney: many, however, show changes pointing to a previous capsulitis. The few functional corpuscles remaining are little altered, except for some dilatation of the capsular space; in some there is slight proliferation of the capsular epithelium and hyaline change in the capillaries of the tuft. There is extreme tubular atrophy of the cortex, which measures 3 mm. Intermixed with the areas of simple atrophy, are small patches showing Chronic Parenchymatous Nephritis. Many of the atrophied tubules contain small hyaline casts. The arteriæ arciformes show considerable thickening, and slight intimal sclerosis: in individual arteries, however, the change is much greater. The interlobular arteries are similarly diseased, often in extreme degree, with great narrowing and even obliteration of the lumina. In some vessels the thickening is very cellular, suggesting syphilis.

Case 16.—W. C., formerly in the Royal Navy, but a painter for the last twenty years, æt. 56. Admitted March 8, 1909. Died May 2, 1909. Ward 8, bed 5. Register No. 646. P.M. Register No. 58.

Symptoms.—The patient was admitted with a history of pain between the shoulders, beginning six months previously. There was also slight cough. Shortness of breath and swelling of the feet and legs were noticed a month before admission, and he had been unable to lie in bed recumbent because it increased the breathlessness.

Physical Signs.—Propped up in bed he apparently had no shortness of breath. There was some cyanosis, no wasting, but œdema of the lower part of the trunk and of the lower extremities. The M.I. could not be defined, the cardiac area seemed a little larger than usual, the aortic second sound was exaggerated, and there was a "to-and-fro" pericardial friction sound audible over the sternum: there were no cardiac murmurs. The brachial arteries were tortuous. There was considerable "bronchitis," and besides the general dropsy there was some ascites. Some fluid accumulated at the base of the left lung, and on March 15 was aspirated with relief to the breathing. Attacks of breathlessness supervened. Later on (April 4) the legs were drained by means of Southey's tubes. Gradually the patient became restless, much cyanosed and breathing became very difficult, and the chest was again tapped on April 19. The blood-pressure became subnormal on April 20, the pulse became more feeble and rapid, and the patient's strength became much less: he became unconscious on April 30, and died in a few hours. The temperature only rose above 99° on three separate days: during the rest of the time it was normal or subnormal. Albumen was found in the urine on twenty-one occasions, and varied from "very slight" to $\frac{1}{12}$th: it was absent entirely on three occasions: blood was never noticed in the urine: hyaline and fatty and granular casts were found. There was no report on the condition of the fundus oculi.

P.M. Report.—The body is well nourished; there is marked œdema and some

cyanosis: it weighs 11 st. Free fluid is found in both pleural cavities and in the abdominal cavity. The parietal pericardium is adherent to the visceral pericardium by means of organised lymph which is very hæmorrhagic, on the posterior aspect of the organ: the heart weighs 24 oz.: the left ventricle is dilated and hypertrophied, the mitral orifice admits five fingers easily, and the valve is thickened: the right ventricle is hypertrophied and dilated and the tricuspid orifice admits five fingers: the aortic ring is not dilated: no incompetence of the valve, which is slightly thickened; the mesenteric vessels are slightly thickened: the aorta itself is dilated and the wall is thickened and is very atheromatous. The kidneys weigh $5\frac{1}{2}$ oz. and 6 oz., they are pale, the capsule strips easily, but leaves a finely granular surface: no cysts are visible, the kidney substance is tough, the cortex is slightly and uniformly diminished: the pyramids show streaks of biurate of soda, there is some general congestion of the

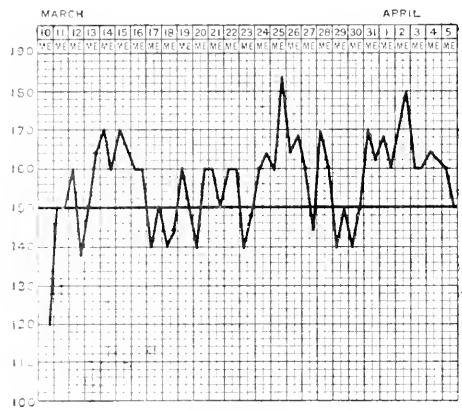


CHART 16.

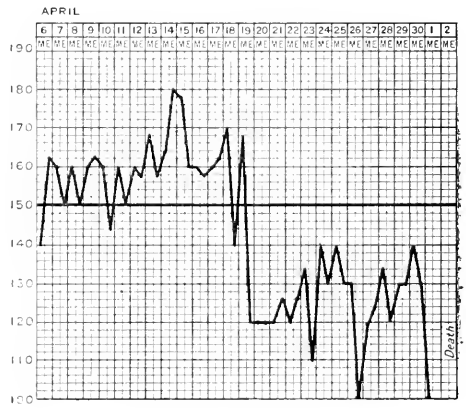


CHART 16 (continued).

kidneys. The small arterioles of the kidney are slightly thickened: the large renal vessels show no narrowing.

P.M. Diagnosis.—Red Granular Kidney, Pericarditis.

Microscopical Examination.—(Kidney not injected.)

Summary.—Slight arterio-sclerosis. Moderate glomerulo-tubular atrophy, apparently independent of the arterial disease, and due to a healed capsulitis.

Details.—The capsule of the kidney is wanting. About 21 per cent. of the Malpighian corpuscles are destroyed, the tufts being small and necrotic and free from hyaline change: the fibrous capsule in almost all shows the lateral thickening due to capsulitis: the functional corpuscles show no change beyond dilatation of the capsules. There is a delicate network of atrophic tubules situated usually in the superficial half of the cortex, and showing intertubular fibrosis. The cortex measures 4·7 mm. Collections of lymphocytes are present in places.

The arciform arteries show moderate thickening of their walls, independent of spasm (I : I+M = 2 : 5), with slight or moderate intimal thickening, not due to "crinkling." The interlobular arteries show similar slight changes.

CASE 17.—E. D., housewife, æt. 40, ward 3, bed 23. Register No. 1033. Admitted pregnant on April 22, 1909, transferred to ward 7, bed 10, on April 27, 1909. Died May 5, 1909. P.M. Register No. 61.

Symptoms.—The patient was admitted pregnant four months, suffering from vomiting, headache and albuminuria. She miscarried, and was transferred to a medical ward. The vomiting and headache, accompanied by nose-bleeding, began a fortnight prior to admission. She had great difficulty in seeing with the left eye, her gums bled freely, and there were purpuric spots all over the body. She had had seven miscarriages and one stillbirth.

Physical Signs.—The patient was semi-comatose at times, and looked very ill. The aortic second sound was accentuated: the M.I. was forcible and dislocated outwards in the sixth space about $5\frac{1}{2}$ inches from the middle line: no murmurs were heard. Fever was present during her stay in hospital (only slight) and albumen was present at each of the four examinations made: blood also was present, and the specific gravity varied from 1010 to 1016. She was a well-built woman. The tongue was of a dark brown colour, and ultimately became dry and swollen. On examination of the urine on one occasion it became nearly solid on boiling and adding acetic acid: there was no record of casts found. There was very slight œdema of the legs, but none over the sacrum; the œdema of the legs ultimately disappeared. The walls of the brachial arteries were "thickened." The margins of the discs were blurred; no hæmorrhages could be seen in either fundus, but white patches were seen in both. Some twitchings were seen in the face. The patient became comatose and died.

P.M. Report.—There is no œdema of the body, no pleurisy or pericarditis. The body weighs 7 st. 7 lb., the heart 14 oz., and each kidney $5\frac{1}{2}$ oz. The left ventricle is dilated and hypertrophied, the coronary arteries show marked atheroma; the aortic and mitral valves are normal. The mesenteric vessels show no thickening, nor do the peripheral vessels. In the pons on the right side in the region of the fillet there is an old hæmorrhage with partially decolorised clot and softening round it. The kidneys are large and finely granular, the capsule is adherent, tearing the substance: numerous small cysts are present; the cortex is slightly narrowed and is pale yellow, showing streaks of fibrous tissue, but scattered throughout the cortex are pale red infarctions and hyperæmic areas: the pyramids are not congested, the arterioles are not appreciably thickened: the renal artery is normal.

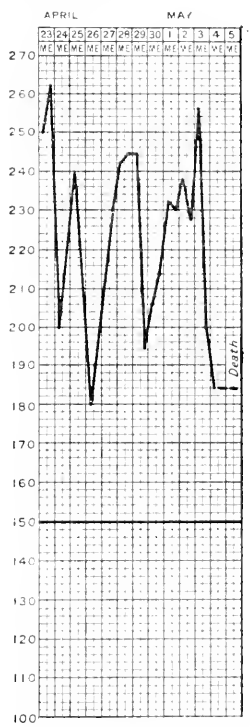


CHART 17.

P.M. Diagnosis.—Chronic Nephritis combined with Acute Nephritis, old Pontine Hæmorrhage and recent Pregnancy.

Microscopical Examination.—(Kidney not injected.)

Summary.—Large areas of intense acute parenchymatous and interstitial inflammation (probably septic). Marked arteriosclerosis. Considerable glomerulo-tubular atrophy, the glomerular destruction probably dependent on an intercurrent capsulitis.

Details.—The capsule is slightly thickened. The cortex measures 5 to 6 mm. The *acute changes* are most marked in the superficial part of the cortex. Here there is cloudy swelling of the epithelium, with desquamation, granular destruction and extensive necrosis of the cells. Blood and polymorpho-nuclear cells are also present in the tubules, either free or within casts. The intertubular tissue is intensely congested, and hæmorrhage and exudation of polymorpho-nuclear leucocytes are frequent. Actual necrosis of the interstitial tissue is met with in many parts: the glomeruli in these areas also show intense congestion, destruction of epithelium and actual necrosis, and many are infiltrated with polymorpho-nuclear cells: some of the vessels in these areas are thrombosed, but no bacterial emboli are recognisable in the glomeruli or vessels.

Chronic changes.—About 11 per cent. of the Malpighian corpuscles are destroyed. The collapsed and necrotic tuft is surrounded by a capsule showing the partial thickening characteristic of a healed capsulitis. The remaining corpuscles are altered by the acute change so that their previous condition cannot be ascertained. Considerable areas of tubular atrophy with fibrosis are scattered through the cortex. There is marked thickening of the inner and middle coats of the arciform arteries in part due to spasm (I : I+M = 5 : 10), and in part to subendothelial fibrosis and to increase of

the thickness of the middle coat ; the interlobular arteries show still greater disease, in many places almost complete occlusion occurring.

Case 18.—(This case, for reasons given later, cannot be considered to be a case of Hyperpiesia.) V. P., charwoman, æt. 71. Admitted May 17, 1909. Died May 21, 1909. Ward 14, bed 18. Register No. 1283. P.M. Register No. 72.

Symptoms.—Whilst walking in the street she became giddy, and then fell quite unconscious. There was a history of some giddiness in the previous week, but no headache.

Physical Signs.—The patient was completely unconscious, the lower eyelids were œdematous, the pupils did not react to light, and there was no conjunctival reflex. Biot's breathing was observed, the right knee-jerk was exaggerated and there were double extensor plantar responses, which were eventually lost. The tongue lay on the floor of the mouth with definite inclination to the right(?). The limbs generally were flaccid. The brachial arteries were tortuous. The funduses of the eyes were normal. Urine drawn off by the catheter on the 17th was normal : on the 19th the urine was found to contain a cloud of albumen. The M.I. was present in the fifth space, was displaced a little to the left of the normal, visible and very forcible ; pulse-rate 56. Lumbar puncture revealed the fact that the cerebro-spinal fluid was freely mixed with blood. The patient died comatose with a temperature of 104°·8 : pulse 120 : on admission her temperature was subnormal, but on the following day rose to 101°·8, fell to 99° the day after that, and then steadily rose till death.

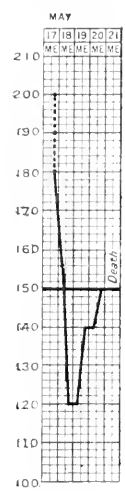


Chart 18.

P.M. Report.—The body is that of a very poorly nourished woman. There is no œdema, but there is marked cyanosis. The body weight is 6 st. 7 lb. A large hæmorrhage is present in the brain, in the region of the right internal capsule : it has passed into the lateral ventricle and has reached the third ventricle. The heart weighs 11 oz., the muscle shows marked "brown" atrophy. The mitral valve is stenosed, only admitting two fingers : the coronary arteries are markedly atheromatous, there is no thickening of the mesenteric arteries, the radial arteries are normal. The kidneys are slightly smaller than normal, the right weighing 3½ oz., and the left 4½ oz. : there are cysts present, the capsule strips off easily, leaving a granular surface : the cortex is pale and is fairly soft, but it is diminished to half the usual size. Stones were found in the gall-bladder.

P.M. Diagnosis.—Renal Disease ; Coronary Atheroma ; Right Capsular Hæmorrhage ; Secondary Rupture into the Ventricle ; Cholelithiasis : Mitral Stenosis.

Microscopical Examination.—(Kidney not injected.)

Summary.—Senile kidney. Slight glomerular destruction and consequent tubular atrophy. Arterio-sclerosis in some of the arteries. The glomerular destruction is apparently due to a past capsulitis.

Details.—The capsule shows slight thickening. The cortex measures 5 mm. in depth, and the arteries of the boundary zone are small. In general the kidney is healthy, though the amount of renal substance is small. About 8 per cent. of the Malpighian corpuscles are destroyed, the destruction being apparently due to a past and healed capsulitis. Associated with these atrophic corpuscles are small areas of tubular atrophy with fibrosis, both being very slight. Some of the glomerular corpuscles show slight hyaline thickening. In addition to the small size of the arciform arteries there is slight arterio-sclerosis, in part due to "crinkling." In the intertubular arteries the same condition is present, and in individual arteries it is marked, but on the whole the arterial changes are slight. Small collections of lymphocytes occur in places.

Case 19.—E. I., porter, æt. 43, ward 8, bed 18. Register No. 1214. P.M. Register No. 77. Admitted May 11, 1909. Died May 28, 1909.

Symptoms.—The patient was admitted for vomiting of blood. He had been unable to work for three months, owing to weakness: wasting had been noticed for two months, and pain in the abdomen had been noted for five weeks. He had been a moderate drinker.

Physical Signs.—There was no dropsy, but the face was puffy and pale: there was an invisible M.I. felt in the fifth space ¼ inch internal to the nipple line: a faint apical systolic murmur; the aortic second sound was not accentuated. The gums bled readily: petechiæ were present on the arms. The brachial arteries were a little tortuous. The patient had been invalided from the Indian Army sixteen years previously for "kidney disease." Death took place from what appeared to be an infection with purpuric manifestations, the infection taking the form of broncho-pneumonia. Albumen was present in the urine: specific gravity 1011 to 1015, quantity 20 to 90 oz. a day. Retinæ normal. No record of fever. The blood count showed secondary anæmia.

P.M. Report.—The body is that of a well-built man, and there is no dropsy. It weighs 10 st. 2 lb. The heart shows no pericarditis: the left ventricle is greatly hypertrophied, the muscle substance is normal, the aortic and mitral valves are free from endocarditis, the coronary arteries are wide and show scarcely any atheroma: the aorta shows very little thickening, and there are very few atheromatous patches: the brachials and carotids are dilated and show very few atheromatous patches, and the mesenteric vessels show no thickening: the dorsales pedis and femoral arteries are slightly thickened: the heart weighs 20 oz. The kidneys are small, weighing 3 oz. each, the surfaces granular, the capsule strips with comparative ease: in the right kidney there are two large cysts, one at either pole, 1¼ inches in diameter: in the left kidney there are a few much smaller cysts: the cortex of each is diminished to ⅛th of an inch, it is pale, but not very tough: the renal arteries are slightly thickened, the main arteries of the kidney are not thickened. Recent lymph is found at the apex of the lower lobe of the right lung: broncho-pneumonia is present in the lower lobe. No disease of stomach or liver.

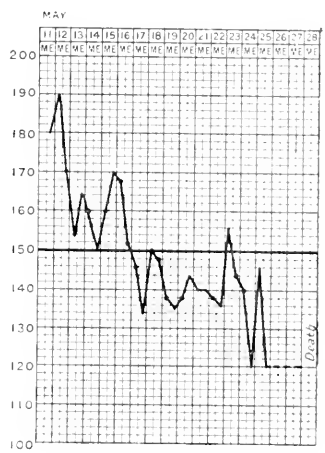


CHART 19.

P.M. Diagnosis.—Red Granular Kidney, Broncho-pneumonia.

Microscopical Examination.—(Kidney not injected.)

Summary.—Marked arterio-sclerosis, great glomerular destruction and tubular atrophy resulting.

Details.—Very few functional Malpighian corpuscles are met with in the section (10 per cent.). Almost all the corpuscles are destroyed; they are greatly reduced in size and the tuft is necrotic without thickening of the capsule. There is very extensive tubular atrophy, only a few scattered islands of normal cortical tubules remaining. The cortex measures 3 to 4 mm. Fibrosis is fairly diffuse among the atrophic tubules, but is more marked in some places than in others.

The arteriæ arciformes are thickened, due to spasm or proliferation (I : I+M = 6 : 13), and there is a thick subendothelial fibrous deposit, apparently in part due to "crinkling." The interlobular arteries show the same change, often in extreme degree. Lymphocytic exudation is present in places. There is much capillary congestion, especially of the boundary zone, and the tubules of the medulla contain blood. The capsule of the kidney is wanting.

CASE 20.—H. R., carman, æt. 42. First admission December 28, 1908. Discharged January 30, 1909. Ward 6, bed 4. Register No. 3472.

Symptoms.—Eight months prior to admission he began to be short of breath, and had pains in the joints (? gout).

Physical Signs.—He was a big man and showed very marked orthopnœa and cyanosis: there were tophi in the ears. There was considerable œdema of the legs and body; the heart was hypertrophied—the M.I. was forcible and present in the sixth space in the anterior axillary line, the aortic second sound was accentuated. There was a large number of moist sounds heard in the lungs; the lower margin of the liver could be felt below the costal margin. Dyspnœa was so great that he was bled on the day of admission and with considerable relief. There was some dullness at both bases behind, the pulse was frequently irregular. The patient gradually improved, the pulse became regular, and the colour improved; the signs of the enlargement of the liver disappeared, the dullness at the bases lessened and the œdema and ascites passed off, and he was discharged to a convalescent home. The temperature was normal throughout the whole stay. The urine was examined five times, albumen was found as a trace or cloud on four occasions, and was absent on another: casts were looked for and could not be found. There was no report on the funduses of the eyes.

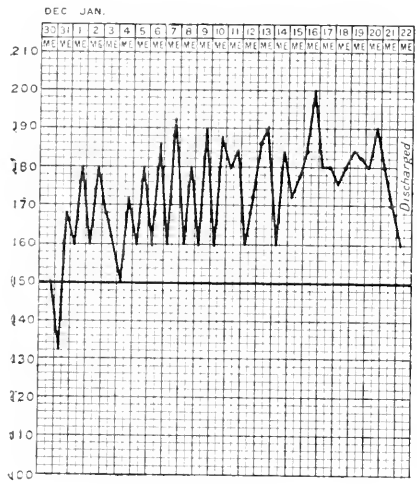


Chart 20A.

Second Admission.—March 3, 1909. Died June 26, 1909. Ward 8, bed 11. Register No. 594. P.M. Register No. 90.

Symptoms.—The patient was readmitted with extreme œdema, with signs of cardiac failure and great breathlessness on the slightest exertion, and even lying down.

Physical Signs.—These were much as they were on the former admission. Cyanosis and pallor were great features, and he had to be propped up in bed. The M.I. as before was localised and somewhat heaving, and present in the sixth space, 6 inches from the middle line: the aortic second sound was sharp: there were no murmurs: the pulse was regular and the brachial artery tortuous. The lower edge of the liver on this occasion reached almost as far as the umbilicus. Insomnia was a marked feature, and there was considerable accumulation of moist signs in the lungs and dullness appeared at both bases of the chest at the back, and ascites developed. Southey's tubes were used to drain off the œdema on May 27, and large quantities of fluid were removed in this way, with temporary relief of the œdema, which, however, recurred, and drainage was again carried out. There was no albuminuric retinitis. Hyaline casts were present in large numbers, and a few granular casts. The urine was examined on forty-seven occasions and albumen was always found to be present

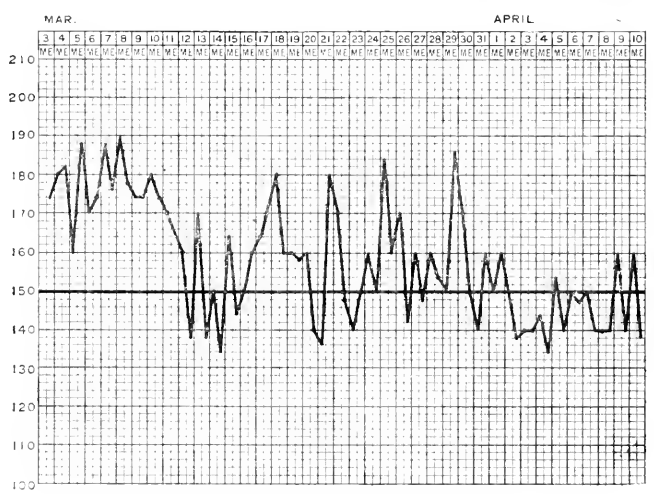


Chart 20B.

in quantities ranging from a trace to $\frac{1}{12}$th to $\frac{1}{3}$rd. The temperature was either normal or subnormal throughout the illness, except on three separate days, on which it never reached more than 99°·4. Tophi were present in the ears. Drowsiness eventually developed and urgent dyspnœa, the pulse became feebler and the expectoration blood-stained, a "to-and-fro" friction sound was heard near the heart. Muscular twitching developed, and the patient gradually sank and died comatose, after being in the hospital 115 days.

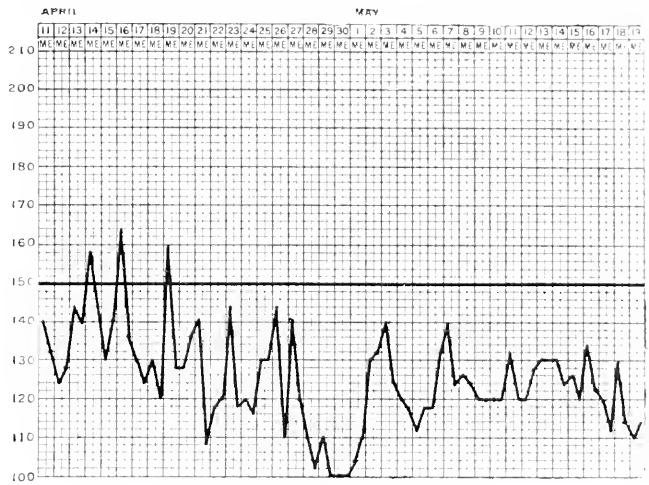


CHART 20B (continued).

P.M. Report.—The body is that of a well-built man, there is marked œdema of the lower extremities and body, and also cyanosis. The body weighs 11 st. 4 lb. The left pleural cavity contains an empyema of 5 pints, several infarcts are present in both lungs, some quite large and inclined to break down. The heart weighs 23 oz., the left ventricle is hypertrophied and dilated and an ante-mortem clot is present at its apex: the coronary arteries are very atheromatous and their lumen diminished: numerous atheromatous patches are present in the aorta: the mesenteric vessels show scarcely any thickening: the peripheral vessels appear normal: the mitral valve is free from endocarditis, but the orifice admits four fingers: the right ventricle is hypertrophied and dilated, the tricuspid orifice admits five fingers, and is free from endocarditis: the aortic valve is normal. The kidneys weigh $4\frac{1}{2}$ oz. each: they are of normal size, but the surface is irregular from recent and old infarcts and is lobulated: the capsule is slightly thickened, and when stripped off tears the kidney substance; the unscarred surface of the kidney is slightly granular; no cysts present; the cortex is of normal size, there is some cloudy swelling and the Malpighian corpuscles are large and hyperæmic. There was no cirrhosis of the liver.

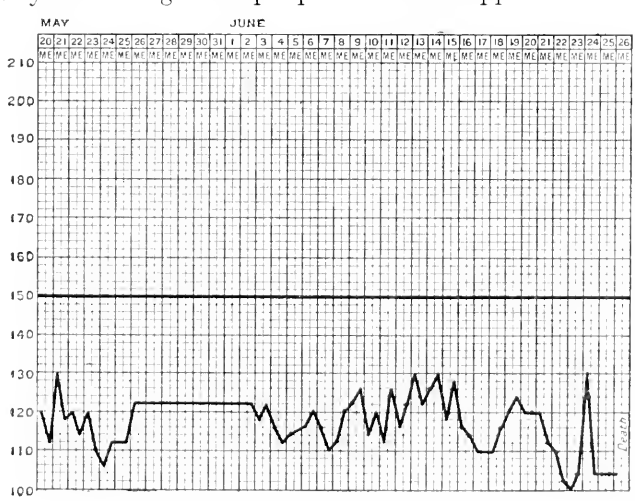


CHART 20B (completed).

P.M. Diagnosis.—Red Granular Kidney (also "Scarred"), Dilatation of the Heart, Infarction of Heart Walls, Infarction of the Lungs and Kidneys, left Empyema.

Microscopical Examination.—(Kidney injected.)

Summary.—Slight glomerular destruction of doubtful origin, and corresponding

tubular atrophy. Slight arterio-sclerosis almost confined to the larger vessels. General cloudy swelling of the tubular epithelium.

Details.—The capsule of the kidney is slightly thickened. The cortex measures 6 mm. About 12 per cent. of the Malpighian corpuscles are destroyed, the tuft being greatly reduced in size and necrotic, and its vessels free from hyaline disease: the capsule is not thickened. Corresponding to the glomerular atrophy are small areas of tubular atrophy with slight intertubular fibrosis. A small amount of lymphocytic exudate is present in places. The functional glomeruli are much congested and their capsules dilated, in some instances containing colloid material. The arteriæ arciformes show a very trifling thickening, not due to spasm (I : I+M = 0·5 : 1·5), but due to a subendothelial deposit. The smaller arteries are practically normal.

Case 21.—(This case, for reasons given later, cannot be considered to be a case of Hyperpiesia.) M. S., a nurse, æt. 35, ward 14, bed 5. Admitted September 24, 1909. Died September 25, 1909. Register No. 2339. P.M. Register No. 140.

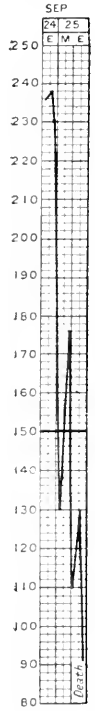


Chart 21.

Symptoms.—"Five days before admission she was in her usual health, and went to visit some friends in the country; she became suddenly unconscious, and has remained so ever since." She was not known to have had any fits; it was ascertained that she had been very liable to headaches and to have been for a long time in the habit of getting up at night to pass water, sometimes four times: she had formerly been operated on for empyema. Her grandfather had had a stroke during middle life: an aunt and a cousin had also had strokes, but the nature of all three strokes was unascertainable.

Physical Signs.—The patient was comatose on admission and could not be roused: she was of good colour. There was left-sided hemiplegia: both knee-jerks were present; both plantar responses were extensor: Kernig's sign was found in both legs. The pupils were artificially dilated, and posterior cataracts were found in both eyes; the retinal veins were a little full; there was some retinitis, but there were no hæmorrhages, the disc was of good colour and had sharp edges, and there was no swelling or filling up of the optic cup: the retinal arteries showed a "silver wire" appearance. "The brachial artery wall was 'felt.'" The M.I. of the heart was thumping in character and felt 4 inches from the middle line (? space): no murmurs were heard; the aortic second sound was accentuated. The urine was examined once and was found to contain a heavy cloud of albumen, and no blood. The breathing became harsh in character, and in a few hours the patient died. There was no fever or dropsy. Lumbar puncture showed cerebro-spinal fluid clear and at low (?) tension.

P.M. Report.—The body is fairly well nourished and weighs 6 st. 2 lb.: no dropsy. A large hæmorrhage is present in the right hemisphere of the brain, near the Island of Reil, this does not extend into the lateral ventricle nor into the internal capsule. The arteries at the base of the brain show no thickening except in the Sylvian branch. The perforating vessels do not appear to have any miliary aneurisms. There is early meningitis. The kidneys are pale, each weighing 2½ oz., the capsule strips with difficulty, tearing the surface, but the surface is not granular: there are no cysts present: the cortex is pale and of normal size and not tough: the Malpighian corpuscles stand out prominently as bright red objects. The heart weighs 9½ oz., there is slight hypertrophy of the left ventricle, the aortic and mitral valves are normal. The coronary arteries are not narrowed, but are markedly atheromatous. The aorta is markedly atheromatous in the whole of its extent: there is no calcification of the atheroma. The other arteries of the body show no thickening.

P.M. Diagnosis.—Cerebral Hæmorrhage; Meningitis.

Microscopical Examination.—(Kidney not injected.)

Summary.—Arterio-sclerosis, considerable only in some of the branches, not in the

larger, in the boundary zone. No recognisable changes in the cortex resulting from this. A few glomeruli in process of capsulitis or destroyed by a past capsulitis; slight tubular atrophy resulting.

Details.—The capsule is normal. One per cent. of the Malpighian corpuscles are destroyed, either by hyaline degeneration, or past capsulitis: it is not quite evident which.

One per cent. of the corpuscles are in a condition of active capsulitis and peri-glomerulitis. There is marked proliferation of the capsular epithelium with abundant lymphocytic exudate around the corpuscles. Ninety-eight per cent. of the corpuscles are normal, except for dilatation of the capsule. The cortex measures 6 mm. A few minute patches of tubular atrophy with fibrosis are present in the cortex. The vast majority of the tubules show no change except some cloudy swelling.

Lymphocytes are absent except around the inflamed glomeruli, as mentioned above. The arteriæ arciformes are much thickened, due to spasm, and show a slight intimal fibrosis, possibly due to "crinkling." Some of the branches arising from the larger arteries of the boundary zone have a much more marked intimal thickening. In the interlobular arteries the change again becomes slight.

Case 22.—A. W., hot-water fitter, æt. 37, ward 6, bed 8. Register No. 1366. First admission May 25, 1909. Discharged June 8, 1909.

Symptoms.—Two months prior to admission he noticed shortness of breath and

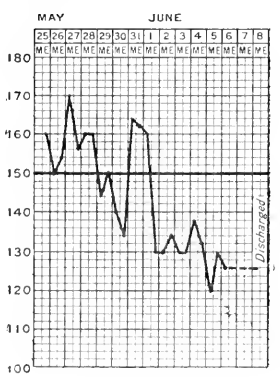


Chart 22A.

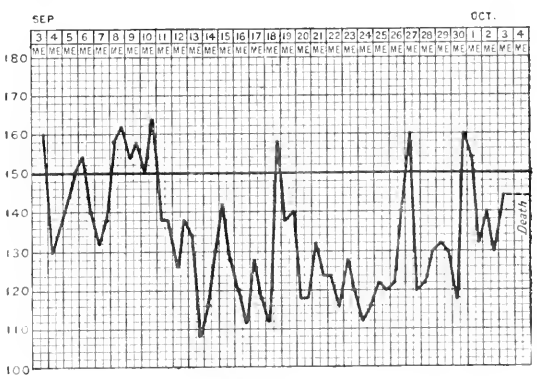


Chart 22B.

weakness; he had had sickness in the morning for a month before admission: these symptoms increased gradually until admission. There was frequency of micturition for the previous two years. His mother had died of apoplexy.

Physical Signs.—On admission he was found to be a powerful man: he appeared to be rather drowsy. The brachial artery was not easily compressible, and could be felt between the beats. The M.I. was in the fifth space just internal to the nipple line, being quite invisible and only felt with difficulty: the second aortic sound was loud, there were no murmurs. There was no dropsy and the funduses of the eyes were quite normal. The temperature throughout his stay was normal except on two days, when it reached about 99°. The urine was examined once, and a cloud of albumen found. As the patient improved he was allowed to go home. Diagnosis, "interstitial nephritis (lead)."

Second Admission.—September 3, 1909. Ward 6, bed 9. Died October 4, 1909. Register No. 2170. P.M. Register No. 143.

Symptoms.—The patient was readmitted with the following history, that four days before readmission whilst at work he felt his arms suddenly "shake about," and then he lost consciousness and fell. He was unconscious for half an hour. In the evening of the same day he had a similar attack, and was unconscious for one hour.

During these fits he struggled violently and once bit his tongue. The fits seemed to come on without any previous malaise or constipation or alteration in the output of urine. The patient was regularly visiting the wards for observation since his last admission. He was said to have had a " blue line " at the age of 20 : only occasionally had he worked with lead. He had had rheumatism fourteen years ago, and syphilis twenty years ago. No scarlet fever.

Physical Signs.—He looked somewhat pale, and otherwise his condition was much as it was when he left the hospital three months previously after his first visit. There were no signs of enlargement of the heart. There was a faint diastolic murmur over the front of the sternum at the level of the third cartilage. The patient was drowsy and complained of thirst. The breath was very offensive, and the tongue covered with greyish yellow fur. Vomiting was a feature during a part of his stay. A small hæmorrhage was found just above the disc in the left fundus oculi : a small patch of exudate was also found in the right fundus oculi (September 4). There was inability to sleep, and on September 21 the uræmic manifestations steadily increased, sickness being a great feature. Twitching of the legs and arms also developed, and he became unable to pass urine from retention. Ultimately the urine became suppressed, he became more and more drowsy, his breathing more laboured, and he died on October 4, comatose. Twitchings had been constantly present. The temperature was changeable, varying from subnormal to 99° on several occasions. On many occasions it did not reach normal at all any day, and on one occasion only it was 100°·2. The urine was examined sixteen times and albumen was found on twelve occasions, and varied from a trace to a faint cloud to a heavy cloud of $\frac{1}{5}$th : hyaline and granular casts were present : it was frequently smoky, due to the presence of blood. There were purpuric spots on the skin.

P.M. Report.—The body weighs 8 st. 2 lb., and is that of a fairly well-built man. There is no œdema, but marked cyanosis. The heart shows no pericarditis, and weighs 12½ oz. : the left ventricle wall is of normal (?) thickness, there is some thickening of the aortic valves at the attached margins : there is some atheroma at the entrance to the coronary arteries : there are numerous patches of atheroma in the arch of the aorta, the mitral orifice and valves are normal, the right ventricle is dilated. The kidneys weigh 3 oz. each : they are small, finely granular, the capsule strips off easily, there are small cysts present ; the cortex is uniformly diminished to $\frac{1}{8}$th of an inch, and is fibroid and fatty. The lower and upper parts of the right lung are solid and friable.

P.M. Diagnosis.—Red Granular Kidney. Pneumonia.

Microscopical Examination.—(Kidney injected.)

Summary.—Chronic glomerulo-tubular nephritis. Marked destruction of glomeruli as the result of the capsulitis, resulting tubular atrophy.

Arterial disease trifling.

Details.—There is slight thickening of the capsule of the kidney. The cortex measures 5·5 mm. About 5 per cent. of the Malpighian corpuscles are normal ; about 25 per cent. are diseased, though still functional, the changes being cloudy swelling or proliferation of the capsular epithelium, with partial adhesion of the capsule. In some of these there is slight hyaline change in the capillaries. The destroyed corpuscles (70 per cent.) mostly show the lateral thickening of the capsule, indicating a healed capsulitis ; in addition some of them show hyaline change in the tuft.

The cortex has a few islands of unaltered tubules corresponding to the healthy glomeruli. Almost the whole cortex shows tubular changes, and of two kinds, which are generally intimately intermixed, but in places separate. The two kinds are (1) atrophy of the tubules, (2) chronic tubular nephritis, with irregular tubules and cloudy and deformed epithelium. Fibrosis is well marked, especially in the areas of chronic tubular nephritis. Lymphocytes occur in considerable numbers.

The arciform arteries show a very trifling subendothelial fibrosis, not due to " crinkling " (I : I+M = 0 : 2), and the wall is otherwise not thickened either by spasm or proliferation. The interlobular arteries are on the whole just as little altered ; but in one or two there is some hyaline change, which may be considerable.

CASE 23.—H. S., cab-driver, æt. 69. Admitted February 21, 1910. Died February 25, 1910. Ward 6, bed 22. Register No. 569. P.M. Register No. 36.

Symptoms.—He was admitted for a general feeling of illness. He had been under observation as an out-patient—one observation on the blood-pressure registered 244 mm. —and had had giddiness for six months. He had never fallen nor lost consciousness: after muscular effort he always felt confused. There had been a little frequency in passing water, and recently he had noticed some shortness of breath and his appetite had failed. Vomiting had occurred only once; but lately there had been considerable nausea. He had had gonorrhœa.

Physical Signs.—The patient was rather stout and had a florid appearance. He was decidedly drowsy when admitted, but could be roused to speak. It was difficult to fix the M.I., and all the cardiac sounds were rather faint, probably due to the existence of emphysema: the left border of the heart was displaced outwards $\frac{3}{4}$th of an inch: the first sound at the apex was accompanied by a localised systolic murmur, the aortic second sound was accentuated: the brachial arteries were tortuous. There were a few bronchitic signs in the lungs. Vision appeared to be fairly good: there was no report on the condition of the fundus oculi, nor on the presence of casts in the urine. The urine was examined three times, on February 21, 23 and 24, and was free from albumen or blood; it was somewhat scanty. The temperature was raised for the first three days during his stay in hospital, reaching as much as 101°, and then fell to normal and subnormal. On the early morning of February 25, after having been washed, and without any warning, he died suddenly.

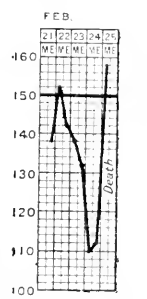


CHART 23.

Note.—As an out-patient, on November 22, 1909, the urine was examined and was found to be free from albumen: on January 31, 1910, it was examined, and albumen was present.

P.M. Report.—The body weight is 9 st. 10 lb., there is no dropsy. The parietal pericardium is adherent to the visceral pericardium: recent lymph is present: the heart weighs 18 oz.: the left ventricle is hypertrophied, and there is some relative incompetence of the mitral valves: there is some slight hypertrophy of the wall of the right ventricle, and there is incompetence of the tricuspid valves: the coronary arteries are markedly atheromatous: in the left one there is a thrombus which blocks the lumen: the area of cardiac muscle supplied by this artery shows a large, yellow-coloured infarct. The right kidney weighs 6 oz., the left $6\frac{1}{2}$ oz.: they are of the large variety of red granular kidney; the capsules are only moderately firmly attached to the substance of the kidney; the surface is typically red and granular, one or two cysts are present: on section the cortex is reduced and the substance of the kidney is friable: there is much fat about the pyramids of the kidney: both renal arteries are markedly sclerotic.

P.M. Diagnosis.—Large Red Granular Kidney, Pericarditis, Infarction of the Heart.

Microscopical Examination.—(Kidney not injected.)

Summary.—Moderate glomerulo-tubular atrophy, due mainly to hyaline arterio-capillary disease.

Details.—The capsule of the kidney is absent. About 22 per cent. of the Malpighian corpuscles are destroyed, the thickened capsule being shrunken upon the necrotic tuft, which in many shows hyaline change: some of the corpuscles show evidence of past capsulitis. About 78 per cent. of the corpuscles are functional and little altered, except for some dilatation of the capsule and thickening of its fibrous layer in some. The cortex measures from 5 to 6 mm., and has a delicate network of atrophic tubules, chiefly in the superficial part: the larger intervening areas of functional tubules have their lumina dilated, containing granular material from the partial breakdown of the cells. In the deeper layers of the cortex there is some cloudy swelling. Delicate tracts of fibrosis occur in relation with the atrophied tubules, and the new tissue is often very hyaline in character. Lymphocytes are few. The arteriæ arciformes show considerable thickening not due to spasm (I : I + M = 2 : 7), and moderate intimal

sclerosis, not due to "crinkling." The same changes occur in the interlobular arteries, and in these and in the afferent arteries hyaline change is very marked.

Case 24.—A. L., æt. 52, cook: single woman. Admitted March 2, 1910. Died July 31, 1910. Ward 14, bed 1. Register No. 674. P.M. Register No. 148.

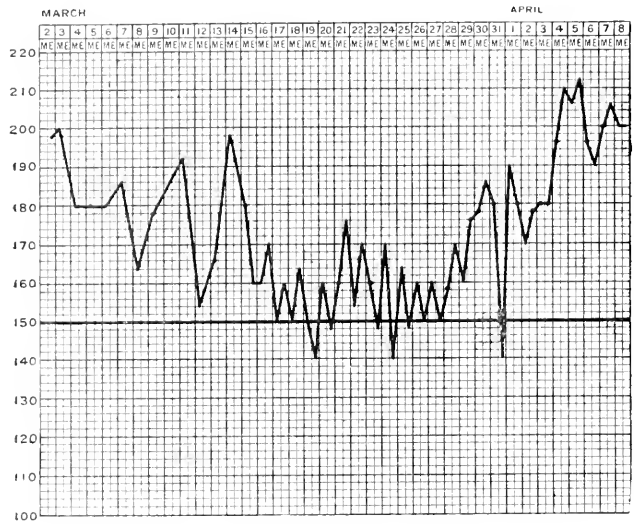


Chart 24.

Symptoms.—The patient was admitted with the history that three weeks previously she had "caught cold in her chest." There was cough, shortness of breath, frequent vomiting, and palpitation. Her legs began to swell, subsequently so much that she had to take to bed, where she had been for eleven days. She had had two previous similar attacks, the first two years ago, and the second three months ago. The phlegm expectorated was never yellow, but white and frothy. Palpitation had been first noticed three years previous to admission. She had had influenza every year for the last seven years. There had been two operations on the pelvic organs, twenty years and two years previously: on the latter occasion the blood-pressure was noted to be 200 mm. She had had rheumatic fever.

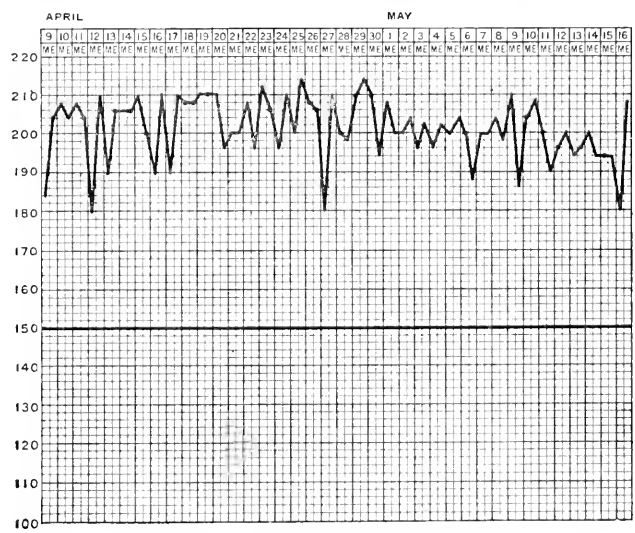


Chart 24 (continued).

Physical Signs. — She was a well-built woman and revealed some orthopnœa, her face was flushed and her eyelids somewhat puffy: her complexion was high coloured and somewhat cyanotic. The conjunctivæ were a little yellow. The pulse was somewhat irregular, and there was some tortuosity of the brachial artery: the M.I. was not forcible, but diffuse pulsation could be felt in the fourth, fifth and sixth space in the left anterior axillary line, the maximum being in the fifth space, 6 inches from the middle line: the area of cardiac dullness was enlarged to the right and to the left: the first sound at the apex was rather short and sharp, and was accompanied by a systolic murmur: there was accentuation of the aortic and of the pulmonary second sounds: reduplication of the second sound was heard at the apex. There was tender-

ness below the right costal margin, and the liver dullness was increased upwards: the edge of the liver could not be felt, nor was the spleen palpable. There was free fluid in the peritoneal cavity, and there was dropsy of the legs, extending well on to the trunk. Examination of the lungs showed signs of emphysema: there was dullness of the left base behind, suggestive of fluid. The urine was examined on nineteen occasions: albumen was present on fourteen occasions, and absent on five: the albumen varied from a faint trace to a thick cloud: the specific gravity varied from 1004 to 1017, the quantity was normal or slightly reduced, except towards the end of the illness, when it was scanty and high coloured, and urates were deposited. The temperature was raised for five days shortly after admission: during the rest of her stay in the hospital it was either normal or subnormal. Vomiting occurred on occasions. The pulse-rate at the time of death was 92 and the respirations 28. On March 8 it was noticed that she was liable to paroxysmal attacks of shortness of breath. During some of these attacks of shortness of breath her pulse became very irregular, and because the attacks became more frequent the left chest was aspirated on April 14, and 18 oz. of fluid were removed. The œdema of the legs and dropsy greatly improved subsequently to this date, and the patient was able to sit up out of bed. On May 27 the attacks of dyspnœa returned and were accompanied by sickness, and fluid was again found at the left base: œdema of the legs and lower part of the body recurred. Aspiration of the left chest was again carried out, and 25 oz. of serous effusion removed. Drainage of the legs by means of Southey's tubes was begun on July 1 but, despite the removal of a large amount of fluid by this measure, the patient remained very short of breath and cyanosed. On July 27 "she had a fit, probably of a uræmic nature," which passed off on the same day. Uræmic fits were repeated several times immediately prior to death on July 31. The funduses of the eyes were

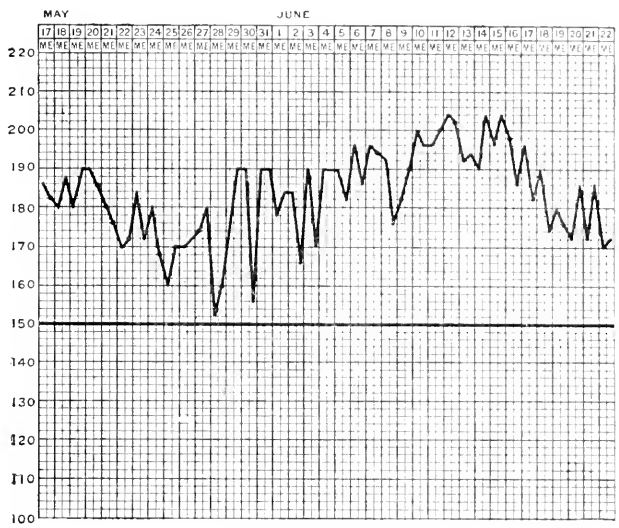


CHART 24 (continued).

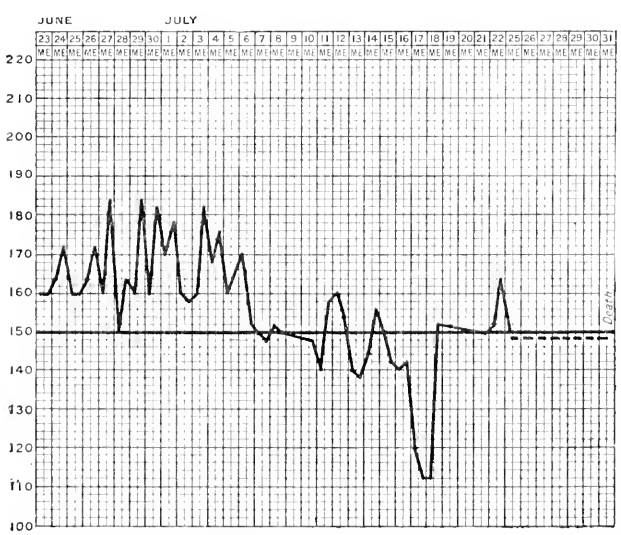


CHART 24 (completed).

examined and showed neither hæmorrhages nor patches of exudation: but the arteries presented the appearance of a "silver wire" condition. Casts were not looked for.

P.M. Report.—The body weighs 9 st. 5 lb.: it is much cyanosed, and there is marked œdema of the legs. The lungs are tough and show brown induration. The heart weighs 20 oz.: the right auricle is dilated and the tricuspid valve admits four fingers: the right ventricle is very hypertrophied and dilated: the pulmonary and tricuspid valves are normal: the left auricle is dilated and hypertrophied, and the mitral aperture barely admits the tips of two fingers and is slit-shaped: the left ventricle is slightly hypertrophied; the aortic valve is normal; there is slight atheroma of the aorta; the mitral valves are thickened, the chordæ tendineæ thickened and short. The liver shows "nutmeg" change. The right kidney weighs 6 oz., and the left 7 oz.; the capsule strips leaving a smooth surface, showing some lobulation: on section the kidney is deeply congested; the cortex is apparently not tougher than normal.

Note.—The clinical diagnosis was "a case of morbus cordis associated with granular kidney, as shown by mitral disease, pleural effusion, hypertension and uræmia."

P.M. Diagnosis.—Mitral Stenosis, Failure of the right heart and back-pressure condition of the organs.

Microscopic Examination.—(Kidney not injected.)

Summary.—Considerable sclerosis, confined, however, to the vessels of the boundary zone and not producing an appreciable effect on the cortex.

Slight tubular atrophy due to destruction of glomeruli, probably by capsulitis.

Details.—The capsule of the kidney is thickened. About 4 per cent. of the Malpighian corpuscles are destroyed, the tuft being small and necrotic and the capsule showing the unequal thickening indicating past capsulitis: 96 per cent. of the corpuscles are normal, except for intense congestion, and some dilatation of the capsules. The cortex measures 6·5 mm., and shows small scattered areas of tubular atrophy, with fibrosis. In many of the non-atrophied tubules the epithelium is cloudy, and contains blood-pigment: in some of the tubes there is much epithelial desquamation, and some contain blood. Small collections of lymphocytes are present, and there is intense general capillary congestion.

The arciform arteries are relatively small (I : I+M = 3 : 5), their walls are thickened, chiefly by a considerable intimal thickening, in places very marked, not due to "crinkling." In the interlobular arteries the sclerosis becomes slight.

Case 25.—M. J., housewife, æt. 40. Admitted September 22, 1910. Died October 31, 1910. Ward 14, bed 6. Register No. 2779. P.M. Register No. 223.

Symptoms.—The patient was admitted with a history that she had had a cough for two months, and that the phlegm was streaked with blood. She had lost weight during the same period, and twice a week for the previous two months she had had nose bleeding. During the same period also she sweated at night. For nineteen years she had had pain over the heart. She had been treated for seventeen years for anæmia. She had had rheumatic fever.

Physical Signs.—The patient was a wasted woman, of pale complexion, very short of breath, and she looked ill. The brachial artery was tortuous. The M.I. was present in the fifth space and was diffuse, and the left border of the heart was external to the left nipple line to percussion: the aortic and pulmonary second sounds were accentuated: there were no murmurs. The breath was offensive: vomiting became a feature during her stay in the hospital, and her sleep was very broken. She had a rigor on September 27. The amount of urine passed was small. On October 2 mucous colitis developed, pain occurred in the front of the heart, and friction sounds were heard there. Some dullness developed at both bases of the chest behind. Vomiting and broken sleep continued, and to this was added great restlessness and agitation. Some œdema developed in both legs and ankles on October 22. On October 27 the left fundus oculi was examined, the artery walls were markedly thickened ("silver wire"), there was no exudate, the edge of the disc was a little blurred, in the right fundus oculi the arteries

were not so much thickened as those in the left: there was no exudate, but the disc was blurred and swollen: no hæmorrhages in either eye. Petechiæ were noticed on the day of death for the first time. The patient became semi-conscious and died quietly. The temperature was normal except on September 26, when she had the rigor, and it reached 101°·4, but soon became normal again, and on the evening of October 1, when it reached 100°. The urine was examined sixteen times, and albumen was always found, from a cloud to 2 per cent.: the specific gravity was always between 1007 and 1012, and occasionally blood was present in the urine: granular hyaline and pus (?) casts were found.

P.M. Report.—The body is very emaciated and only weighs 4 st. 3 lb., and there are scattered petechiæ in the skin. The layers of the pericardium are adherent, the result of recent fibrinous hæmorrhagic inflammation: the heart weighs 13 oz. and is enlarged, the left ventricle is hypertrophied and dilated, and there are one or two small areas of atheroma on the mitral flaps and at the commencement of and throughout the aorta: in all other respects the heart is normal. There is recent pleurisy, which is blood-stained: there are some broncho-pneumonic patches at the base of the left lung. The brachial artery is not (?) thickened, and is healthy. There is congestion of the mucous membrane of the intestines, and small oval ulcers are visible. The liver shows a coarse lobulation on its surface, the lobuli being rounded and about $\frac{3}{4}$ths of an inch in diameter: this lobulation is caused by perihepatitis, probably of syphilitic origin, because the substance of the liver shows no cirrhosis. The splenic artery is slightly diseased and dilated, and on one of its branches is a saccular aneurism of the size of a small cherry. The kidneys are reduced in size, the right weighing 2 oz., the left $2\frac{1}{2}$ oz., the capsule is slightly thickened and adherent, and the surface is red and definitely and finely granular: the cortex is reduced: several arterioles stand out prominently, the renal artery is not especially thickened, the basal arteries of the brain show patches of atheroma scattered at irregular intervals; the fundus of the left eye shows a retinal hæmorrhage.

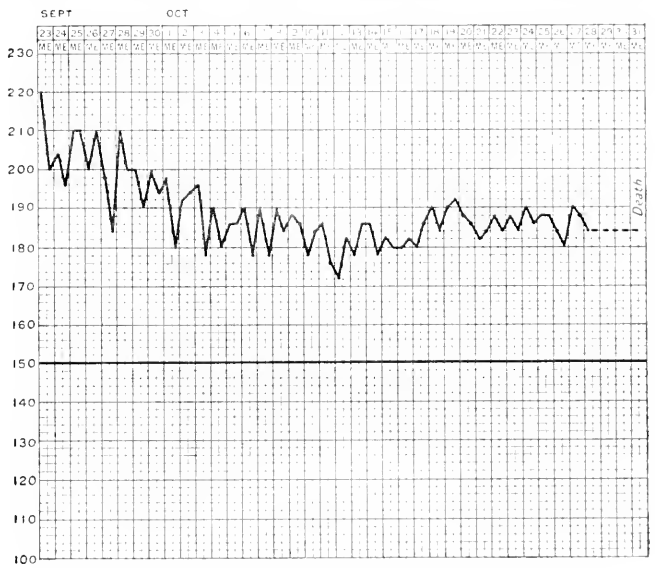


Chart 25.

There is perihepatitis with fibrosis of the liver.

P.M. Diagnosis.—Red Granular Kidney, Acute Pericarditis, Pleurisy, Broncho-pneumonia, Syphilitic Perihepatitis.

Microscopical Examination.—(Kidney not injected.)

Summary.—Marked glomerulo-tubular atrophy. Marked arterio-capillary hyaline disease and sclerosis.

Details.—The capsule of the kidney is thickened. About 30 per cent. of the Malpighian corpuscles are destroyed, the change consisting of atrophy and necrosis of the tuft, with hyaline change, and in places thrombosis of the capillaries: many of the corpuscles also show evidence of a past capsulitis: 70 per cent. of the corpuscles are functional and fairly normal, many of the capsules are slightly dilated, and in one or two

there is hyaline change in the tuft. The cortex measures 4 mm., and contains thick tracts of atrophic tubules, with fibrosis. The intervening islands of functional tubules show partial granular disintegration of the epithelium. Lymphocytic exudate is abundant in places. The arteriæ arciformes show moderate thickening of the wall not due to spasm (I : I+M = 1 : 6), with slight intimal sclerosis, independent of "crinkling." The interlobular arteries show similar changes, but in places the disease is extreme and hyaline change is marked. In one or two vessels the deposit is very cellular, suggesting syphilis.

Case 26.—A. E., cook, æt. 45.

Symptoms and Signs from 1902 to 1908.

1902.—She first came under observation at the age of 37, in the year 1902. She then complained of palpitation for twenty years which had become worse, of slight and recent cough, and that she expectorated yellowish phlegm. Her husband had been treated for hæmoptysis and had died of tuberculosis. The patient noticed that her ankles occasionally swelled, and she generally had to get up at night to pass water. The M.I. was noticed to be diffuse and a *little external to the nipple line under the fifth rib*.

1908.—Six years later the patient came again complaining of slight cough in the morning: the expectoration was white or yellow, and she was short of breath on exertion: occasionally she had brought up a streak of blood. She was still in the habit of getting up at night to pass urine, and had a temperature of 99°·2. The M.I. of the heart was observed in *the sixth space external to the nipple line*: the second sounds at the base of the heart were accentuated. There was a cloud of albumen in the urine, and she gave the appearance of being a case of "Hypertrophy of the Heart, Arterio-sclerosis and Granular Kidney."

Two months later râles and some impairment of percussion note were heard over the apex of the right lung: examination (November 7, 1908) of the sputum revealed no tubercle bacilli.

The systolic blood-pressure was, on July 11, 1908, 230 mm.: two months later (September 12, 1908) the pressure was 224 mm., and albumen was found: two months later (November 7, 1908), 206 mm.

1909.—Three months later (February 6, 1909) the M.I. of the heart was found under the *fifth rib of the left side external to the nipple line*, and there were numerous râles to be heard back and front of the right side of the chest. There was no albumen in the urine. The sputum showed no T.B. on March 6, 1909.

On May 8, 1909, she was again examined and a small excavation was found in the right apex in front: the cardiac signs remained the same, except that the right side of the heart began to be uncovered: the blood-pressure was 206 mm. and T.B. were found to be present in the sputum.

The patient was then admitted to ward 7, bed 6, on May 11, 1909, and was discharged on June 26, 1909. Register No. 1213.

Symptoms.—She complained of much the same symptoms as had been observed for the last two months, namely, the coughing up of yellow expectoration and on several occasions of hæmoptysis. She had lost weight very considerably (20 lb. in a year). She often found herself sweating at night.

Physical Signs.—The patient was found to be wasted: obvious signs of involvement of the right lung with pulmonary tuberculosis were present. The *M.I. was present in the fifth space, $2\frac{1}{4}$ inches from the mid-sternal line*, the impulse was localised and forcible: no murmurs could be heard, the second sounds were accentuated. The radial artery could be rolled under the finger. There was considerable fever during her stay in the hospital, reaching as much as 102°, and T.B. were quite numerous in the sputum. Signs of excavation at the right apex became more obvious. On leaving the hospital the right heart had become more uncovered. The urine was examined nine times and revealed no albumen on any occasion: the specific gravity varied from 1009 to 1017: the quantity of urine passed varied from 12 to 52 oz. No report was made on the fundus oculi, nor were casts looked for. The patient was subsequently

admitted to the Brompton Hospital in July 1909, where she remained until October 1909 : no observations made on pressure, or on urine.

She attended in November 1909 as an out-patient. It was then noticed that there were some signs of tuberculosis at the left apex as well as at the right, that the heart was dislodged to the right, and the M.I. was *just internal to the left nipple line*. The blood-pressure on November 13, 1909, was 174 mm. A year later (September 21, 1910) the blood-pressure was 175 mm., and the urine was free from albumen. The physical signs in the lungs and the heart were much the same as noticed in November 1909, the M.I. being *again noticed internal to the left nipple line.*

The last admission to hospital was on October 28, 1910. Died November 5, 1910. Ward 14, bed 8. Register No. 3201. P.M. Register No. 230. Æt. 45 years.

Symptoms.—She had become excessively weak during the previous four days and was unable to walk. Cough was still present, as well as headache.

Physical Signs.—She was found to be very wasted and her breath was offensive ; there was pyorrhœa. There was œdema over the sacrum and in both legs. The brachial arteries were tortuous. The M.I. was in the *fourth space internal to the left nipple line.* The dullness of the right border of the heart was lost in the dullness of the consolidated

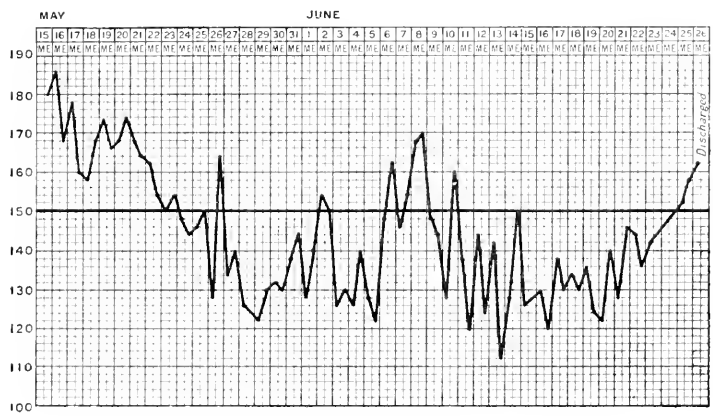


Chart 26a.

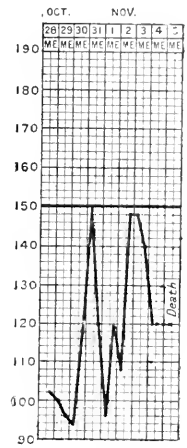


Chart 26b.

right lung. The aortic second sound was accentuated : there were no murmurs. There were signs of extensive pulmonary tuberculosis in the right lung, and less in the left. There was no report on the fundus oculi : a few hyaline and fatty casts were found, and during her nine days' stay in the hospital there was fever. The urine was examined twice, and albumen found. The patient died of exhaustion.

P.M. Report.—There is œdema of both lower extremities, and the body weighs 7 st. 8 lb. The heart is slightly enlarged, weighing 14 oz. : the tricuspid orifice is slightly dilated, the valve being normal : the mitral orifice is of normal size, the edges of the flaps are slightly thickened, also the chordæ tendineæ : the left ventricle is slightly hypertrophied and dilated, there are scattered patches of atheroma in the coronary arteries : the heart muscle is pale and friable : the pericardium is normal. There is extensive tuberculosis of the right and left lung, especially of the right. The kidneys are large, the right weighing 7 oz. and the left 8 oz. : the capsules are slightly thickened and slightly more adherent than normal : one minute retention cyst is present on the surface of one kidney, which is smooth except for embryonic lobulation and a few small infarction scars : on section the organ is congested ; the cortex is wide, the pyramids purple : the consistence is somewhat increased.

P.M. Diagnosis.—Pulmonary Tuberculosis.

Microscopical Examination.—(Kidney not injected.)

Summary.—Slight patchy chronic interstitial nephritis. Slight arterio-sclerosis. General cloudy swelling.

Details.—The capsule of the kidney is wanting. Almost all the Malpighian corpuscles are normal, except for slight dilatation of the capsules. The cortex measures 7·5 mm. The tubules are slightly distended, and the epithelium is swollen and undergoing partial granular disintegration. A few small areas of atrophic tubules with and without fibrosis are scattered through the cortex, and these are somewhat more marked in the situation of irregular scattered depressions met with on the surface of the kidney. Some of these areas extend from the capsule to the boundary zone and even deep into the medulla, and the capillaries in them are markedly dilated. Lymphocytes are present in some places, but not in great numbers. There is moderate thickening of the middle coat of the arteriæ arciformes, dependent in part upon spasm (I : I+M = 1 : 5), with slight intimal thickening, in part due to "crinkling." The smaller arteries are normal.

Case 27.—(This case, for reasons given later, cannot be considered to be a case of Hyperpiesia.) K. C., housewife and cook, æt. 32, ward 7, bed 23. Admitted November 4, 1910. Died November 16, 1910. Register No. 286. P.M. Register No. 236.

Symptoms.—The patient was admitted for vomiting and drowsiness and swelling of the abdomen of three weeks' duration. She had had headache also for a week. The vomiting was a feature first thing in the morning. She had occasionally vomited bright red blood. The headache had kept her awake at night. There was a history of excessive alcoholism. She had had no children, and there had been no miscarriages.

Physical Signs.—The patient was a stout woman of normal complexion. The M.I. was present in the fifth space in the nipple line, and was not forcible : there were no murmurs. There was no fluid in the abdomen. She was highly nervous, and there was a tremor of the hands. The vomiting of blood continued whilst she was in the ward. On November 10 her respirations fell to four or five a minute, and the temperature was below 96° and the pulse over 100 and very weak. The breath was "uræmic" in character and the pupils small. She was very drowsy, and there was occasional twitching of both the upper and lower limbs and mouth ; she passed only 3 oz. of water in the last twenty-four hours of life. The above condition of drowsiness continued for a day, but it was less marked and the patient refused to take food, which had to be administered with a nasal tube. Three days before death she had an epileptiform fit, lasting ten minutes. The same symptom occurred on November 14, and on the 15th she was very restless and noisy, showed a tendency to twitch, and died on the 16th. The temperature was normal except for the last thirty-six hours, when it rose to 100° and 100°·2. The urine on the first examination showed no albumen, but it was present on the next two occasions on which it was examined : there was no dropsy. There was no report on the presence or absence of casts, on the condition of the brachial artery, or on the condition of the funduses. The autopsy notice was "Cirrhosis of Liver and Uræmia."

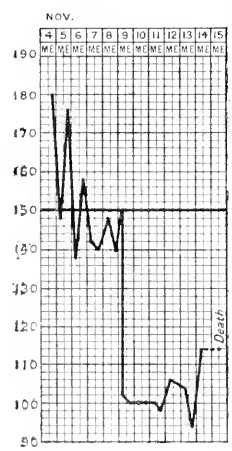


Chart 27.

P.M. Report.—The body weighs 8 st., and there is much fat present. There is nothing abnormal in the heart, except friability and softness of the muscle : no hypertrophy of the left ventricle, and the aorta and the brachial and radial arteries are normal. The pleuræ are adherent in places, the lungs show congestion and consolidation, and the trachea and bronchi are congested. The liver is of normal size, free from cirrhosis, smooth on the surface and mottled with pale areas. The heart weighs 8 oz. Each kidney weighs 5 oz., and is of normal size : the surface is marked by numerous irregular scar-like depressions : between these depressions the renal substance is smooth and normal in appearance : one or two cysts project on the surface : on section there is

loss of kidney substance, corresponding to the surface depressions: elsewhere it appears normal: several scattered infarcts of small size are seen on the surface of both kidneys. There is considerable cystitis, and double pyosalpinx. The renal artery is not thickened. There are no other abnormalities present in the body.

P.M. Diagnosis.—Broncho-pneumonia, and death possibly due in part to alcoholic poisoning (*vide supra*, "Cirrhosis of Liver and Uræmia").

Note.—During her stay in the ward considerable difficulty had been met with in diagnosis, and her symptoms, taken in conjunction with her history, suggested alcoholic toxæmia, but the onset of fits, mentioned on November 10, and subsequent symptoms suggested uræmia.

Microscopical Examination.—(Kidney not injected.)

Summary.—Marked arterio-sclerosis (patchy): marked glomerulo-tubular atrophy, due to the arterial disease and accentuated by considerable destruction of glomeruli resulting probably from a past and healed capsulitis.

Details.—Capsule of kidney thickened. The kidney has numerous deep depressions in the surface; the histological changes in these are: About 33 per cent. of the Malpighian corpuscles are destroyed, most of these showing the localised hyaline thickening of the capsule, due probably to a healed capsulitis, and the tuft being either atrophied with or without hyaline change, or, in the case of a few, necrosed. About 67 per cent. are functional, but nearly all of these show some compression of the tuft, which is small, rounded, compact, well nucleated, and the capsule shows hyaline thickening of its fibrous layer and dilatation of the space. The atrophy of the tubules is extreme, almost total. Fibrosis is general in places, but is not marked. Cortex, 3·6 mm. Considerable collections of lymphocytes occur in places. The arteriæ arciformes show marked thickening of the middle coat not due to spasm (I : I+M = 4 : 10), and intimal sclerosis not due to "crinkling." The interlobular arteries at their commencement are similarly altered, but towards the surface this diminishes and there is no tendency to obstruction of the lumina.

In the undiseased portion of the kidney the above-named changes are present, but slight: thus, Malpighian corpuscles destroyed, 4 per cent.: functional and normal, except for dilatation of the capsule, 96 per cent.: tubular atrophy and fibrosis are present in mere traces. Cortex, 5 mm. Most of the tubules show swollen epithelium with desquamation. The arteriæ arciformes are scarcely thickened at all (I : I+M = 1 : 8), and the intimal deposit is trifling, not due to "crinkling." The interlobular arteries are practically normal.

Case 28.—J. T. W., brewer's labourer, æt. 46. Admitted October 10, 1910. Died November 12, 1910. Ward 8, bed 18. Register No. 2977. P.M. Register No. 234.

Symptoms.—Six weeks prior to admission he began to be troubled by a bad cough, and a week later he coughed up a pint of bright red blood, which was repeated on two occasions later, but in a smaller quantity. He had also noticed palpitation, shortness of breath on the slightest exertion, and on attempting to hurry became very giddy and faint: after standing for some time he noticed his feet swelled. He passed a large quantity of urine, usually getting up three times at night. He had had no headaches, had had attacks of bronchitis five years and two years ago, but no spitting of blood on these occasions.

Physical Signs.—The patient was a wasted man, free from dropsy, and his complexion was pale. The M.I. could not be seen or felt, but the percussion note indicated that the heart was enlarged to the left: the aortic and pulmonary second sounds were loud and reduplicated. Some fine crepitations were heard over the lungs. The liver was a little tender, and could be felt below the costal margin. Dullness developed at the left base, and on October 21, 28 oz. of straw-coloured fluid were withdrawn. Subsequently dullness developed at the right base, as well as some swelling of the legs. Diarrhœa supervened, and a severe pain was noticed on November 4 over the precordium. A few days later pericardial friction sounds were heard over the heart. The sputum was examined on two occasions, but no tubercle bacilli were discoverable.

Latterly his mental powers became impaired, and he died quietly. The temperature throughout his stay in the hospital was normal or subnormal, even to the extent of not being registerable at all during the last three days of his life: on one occasion only was the temperature raised to a little over 99°. There is no report on the funduses of the eyes, and no report on the examination for casts. His brachial arteries were tortuous. The urine was examined nine times: albumen was present on the first six occasions, reaching as much as 2·5 per mille, and on the last three occasions there was no albumen at all, namely, on November 1, November 5, November 7.

P.M. Report.—The body weighs 9 st., there is some œdema of both legs. There is a layer of recent fibrinous exudation over the pericardium, and there is some blood-stained fluid in the sac: the heart, which is much enlarged, weighs 18 oz., the right ventricle is dilated and hypertrophied, the tricuspid valve is normal, and the orifice slightly dilated: the mitral orifice is of normal size, and the valve is normal, except for two or three patches of atheroma: the left ventricle is dilated and its walls hypertrophied: the aortic orifice and the valves are normal: the aorta shows very small atheromatous patches. The lungs show some scarring of the apices and contain small fibrous and calcareous nodules: there is no report of any active pulmonary tuberculosis: the base of the right lung is congested, and both lungs show signs of bronchitis. The bronchial glands are normal. The kidneys weigh 3 oz. each: they are small, the capsule is thickened, and strips less readily than normal: the surface of the kidneys is red and granular, the cortex is greatly reduced in thickness and very tough: the arterioles are thickened and stand out from the section: the renal artery is not appreciably thickened.

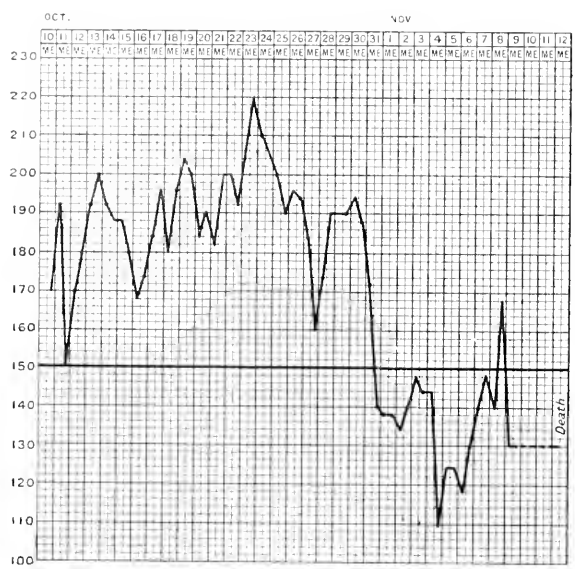


Chart 28.

P.M. Diagnosis.—Red Granular Kidney, and Acute Pericarditis. Bronchitis.

Microscopical Examination.—(Kidney not injected.)

Summary. — Marked arterio-sclerosis and consequent marked glomerulo-tubular destruction, intensified by extensive capsulitis.

Details.—Capsule of kidney thickened. The condition of the cortex varies in different places; where the changes are most severe the Malpighian corpuscles are destroyed in 60 per cent. In those the tuft is generally necrotic and the capsule shows the lateral thickenings of past capsulitis. There is probably also a certain amount of simple anæmic necrosis of the tuft. The destruction is most marked towards the surface of the organ. About 40 per cent. of the corpuscles are functional and normal, except for dilatation of the capsule. In some the capsular epithelium is swollen and in a few there is epithelial proliferation. The fibrous capsule shows slight hyaline thickening in many.

There is great atrophy of the tubules, only a few islands of functional tubules remaining. In the latter the lumina are dilated and the epithelium swollen and disintegrating. In one area the epithelium shows the cloudy changes of chronic parenchymatous nephritis, with surrounding fibrosis. The cortex measures 3 mm.

Fibrosis is well marked in many places, and lymphocytes are present in small col-

lections. There is intense capillary congestion. The arciform arteries are thickened, independent of spasm (I : I+M = 4 : 8), and there is marked intimal thickening, independent of "crinkling." The same change is present in the interlobular arteries and is often extreme.

Changes similar to the above occur in the less diseased parts, but are less marked (Cortex, 5 mm.).

CASE 29.—J. R., painter and house decorator, æt. 64. Admitted November 7, 1910. Discharged November 23, 1910. Ward 6, bed 23. Register No. 3313.

Symptoms.—Shortly before admission the patient began to suffer from shortness of breath in attacks, and had had occasional headaches. He had had scarlet fever as a child: subsequently rheumatism and gonorrhœa.

Physical Signs.—He was a well-built man: he sat propped up in bed: he was very short of breath, the lips rather pale and cyanosed, and there was some œdema of the ankles. The M.I. was felt with difficulty in the sixth space, 1 inch external to the left nipple line: there was increase of the cardiac dullness to the right of the sternum: the aortic and pulmonary second sounds were accentuated: there was cardiac irregularity: the walls of the arteries appeared to be thickened: bronchitic sounds were heard in the lungs: at a subsequent examination the M.I. was found to be in the fifth space in the nipple line, and was forcible and heaving: there was no murmur and the aortic second sound was still accentuated: he felt better and the shortness of breath was less. The funduses of the eyes showed thickening of the arteries, but nothing else abnormal. Before he left the hospital a systolic murmur was heard at the apex of the heart, and a systolic and a diastolic murmur at the aortic cartilage. No casts were found in the urine: a thick cloud of albumen was found on the occasion when the urine was first examined, but on four subsequent occasions no albumen could be discovered. The temperature was normal throughout his stay in the hospital.

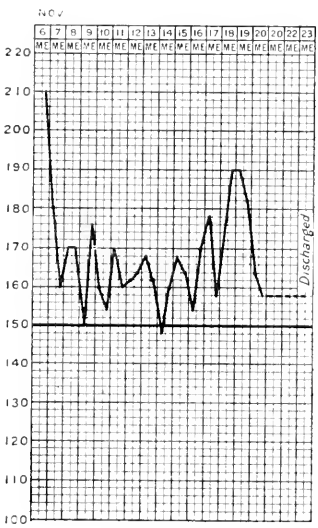


CHART 29A.

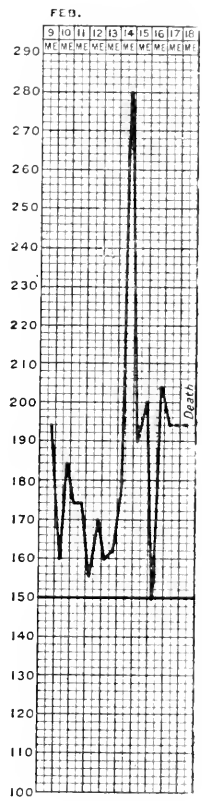


CHART 29B.

Second Admission.—The second admission took place on February 9, 1911, and death on February 18, 1911. Ward 6, bed 15. Register No. 454. P.M. Register No. 32.

Symptoms.—Shortness of breath and giddiness had become very marked for five days prior to admission. Occasionally there was pain over the heart, and he had got up to pass water in the night, sometimes twice.

Physical Signs.—He was a well-developed man, though wasted: was very short of breath in attacks. There was some œdema in the lower part of the body and the legs. The M.I. was present in the fifth and sixth spaces, 4 inches from the middle line of the chest. There were pre-systolic and systolic murmurs at the apex of the heart: two murmurs, systolic and early diastolic, were heard at the aortic cartilage. The lower edge of the liver could be felt 3 inches below the costal margin. The dyspnœa improved very much temporarily: subsequently very severe dyspnœa recurred. Exami-

nation of the eyes showed no changes except pressure on the veins where they were crossed by "silver wire" arteries. The patient became very sleepless and restless as well as very dyspnœic. He died during an attack of laborious breathing. The temperature rose only once to 99°; during the rest of his life it was normal or subnormal. The urine was examined on five occasions, but albumen was found only on the last two: the specific gravity varied from 1025 to 1030, the quantity of urine from 40 to 56 oz.: there were no observations for casts.

P.M. Report.—The body weighs 8 st. 2 lb.: there are a few ounces of bloodstained fluid in the pericardium. The heart weighs 24 oz., the right auricle is dilated, the tricuspid orifice is dilated and the tricuspid valves slightly thickened: the right ventricle is dilated and hypertrophied, the pulmonary artery and valves are normal: the left auricle is slightly dilated; the mitral orifice admits three fingers: the mitral valve and the chordæ are slightly thickened, but competent: the left ventricle is dilated and much hypertrophied, the aortic orifice is smaller than normal: the valve flaps are thickened and retracted. The aorta is dilated in its first part, its wall is much diseased, being thickened and sclerotic: no fatty degeneration or calcification seen: the lower part of the aorta is less affected. There is evidence of some purulent bronchitis in the lungs. The kidneys are congested, the right one weighs 4 oz., and the left is approximately of the same weight; the capsule strips readily, the organs are slightly reduced in size, the surface is red and uniformly and finely granular; the cortex and pyramids are reduced, the substance of the kidney is fatty, the renal arteries are thickened in some places.

P.M. Diagnosis.—Aortic Stenosis and insufficiency; Red Granular Kidney.

Microscopical Examination.—(Kidney injected.)

Summary.—Considerable glomerular atrophy, the effect probably of a past capsulitis resulting in considerable tubular atrophy: moderate arterio-sclerosis—the two conditions probably independent.

Details.—The capsule is slightly thickened. About 26 per cent. of the Malpighian corpuscles are destroyed: they are greatly reduced in size, the tufts necrotic and the shrunken capsule unequally thickened and hyaline: the epithelium of the functional tubules has in most places a cloudy appearance. The cortex is 3 to 5 mm. wide, and shows a delicate network of tracts of atrophic tubules. In most places fibrosis is present, but not in all. Lymphocytes occur in considerable numbers in places.

The arciform arteries are considerably thickened, in part due to spasm (I : I+M = 3 : 7), and show a moderate intimal fibrosis, in part due to "crinkling." The same condition is met with in some of the interlobular arteries.

Case 30.—W. R., æt. 60, insurance agent. Admitted February 9, 1911. Died February 18, 1911. Ward 6, bed 20. Register No. 445. P.M. Register No. 34.

Symptoms.—The patient was admitted with symptoms of lack of appetite and constipation for four months: he had vomited for fourteen days four or five hours after food: there was no blood present in the vomit: the urine was noticed to be scanty for a week before admission. He had had malaria, gonorrhœa and dysentery, and had partaken freely of alcohol.

Physical Signs.—The man was rather emaciated, but his complexion was of good colour, the tongue was furred and inclined to be dry. The abdomen was distended and an ill-defined mass could be felt in the epigastric region. The liver could be felt a finger's width below the ribs. The M.I. was placed beneath the sixth rib, but external to the left nipple line: the second aortic sound was accentuated: no murmurs were heard. The brachial artery was tortuous. He continued to have repeated vomiting, and was treated by lavage. On February 13 fæcal matter was returned in the fluid washed out. Stomach analysis indicated that the case was one of carcinoma ventriculi, and this was confirmed by an exploratory operation. The patient died of inanition on the 18th of the month. The temperature was subnormal until the day of death, when it rose to 99°·4. The urine was examined on four occasions and no albumen was found: the specific gravity was 1020 on the one occasion observed: the quantity was

always reduced, 12, 22, 20, 24 and 28 oz. in twenty-four hours. No report on casts nor on the examination of the funduses of the eyes. There was no dropsy.

P.M. Report.—There is a primary carcinoma of the stomach and diffuse small secondary growths all over the peritoneum, omentum, etc. The body weighs 8 st. 4 lb. The heart is enlarged and weighs 18 oz.: the tricuspid orifice is slightly dilated, the left auricle is slightly dilated, the mitral valves are slightly thickened, but are probably competent: the left ventricle is not appreciably dilated, but its walls are very greatly hypertrophied: the aortic orifice is of normal size, the aortic valves are slightly thickened, but are probably competent. There is extensive atheroma of the aorta. The kidneys weigh 4 oz. each; they are reduced in size, the capsule is a little thickened, the surface is purple-red, is granular and shows small scattered cysts: the cortex is reduced in width, the consistence is increased: the renal artery is not thickened.

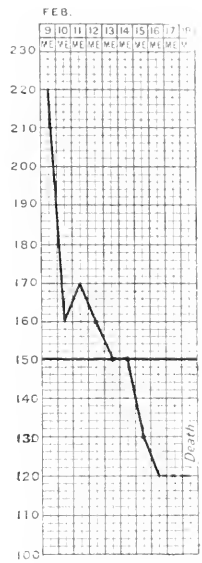


CHART 30.

P.M. Diagnosis.—Carcinoma of the Stomach, Red Granular Kidney.

Microscopical Examination.—(Kidney injected.)

Summary.—Considerable arterio-sclerosis. Considerable glomerulo-tubular atrophy, probably mainly dependent on a past capsulitis and independent of the arterial disease.

Details.—The capsule of the kidney is slightly thickened. About 24 per cent. of the Malpighian corpuscles are destroyed, the tufts small and necrotic, the capsules showing the unequal hyaline thickening of past capsulitis. About 76 per cent. of the corpuscles are normal, except for dilatation of the capsules: in some there is a very slight hyaline change in the capillaries or in the fibrous capsule. The cortex measures 6 mm.

There is a network of atrophic tubules, densest in the superficial layers of the cortex. The functional tubules are a little dilated and show granular destruction of the epithelium. Fibrosis is distinct among the atrophic tubules; and the connective-tissue fibrils between the functional tubules are thickened in many places as if by hyaline change.

Lymphocytes are abundant in places. The arciform arteries are thickened, not due to spasm (I : I+M = 4 : 9), and there is considerable intimal fibrosis, not due to "crinkling." In the interlobular arteries sclerosis is still more marked, but there is no special tendency to obliteration of the lumina.

CASE 31.—M. S., housewife, no children, æt. 37, ward 14, bed 11. Admitted March 14, 1911. Died April 4, 1911. Register No. 821. P.M. Register No. 65.

Symptoms.—The patient was admitted with a history of headache, sickness after meals, and pain in the stomach for six months; also for shortness of breath occurring in attacks and dropsy of the legs for one month. She had noticed that she passed more water than she used to do, and got up at night four to seven times. The menstrual periods had ceased for two months. As a young woman she had always been noticed to be pale, was short of breath on exertion and liable to faint, and yet the menstrual periods were quite normal.

Physical Signs.—The patient was a well-nourished woman who had to sit up in bed because she was so short of breath. There was œdema of the legs and lower part of the body, and she complained of tenderness on attempts being made to test for pitting by pressure. The M.I. was present in the fifth space in the left nipple line: no murmurs were heard. The brachial artery and temporal arteries were not tortuous, but they were felt thickened between pulsations. There were some bronchitic signs in the lungs. The lower margin of the liver was depressed three to four fingers' breadths below the costal margin. Both eyes were examined, but there were no hæmorrhages and no white patches (*see* P.M. Report): the artery walls were thin, the veins full;

there was some haziness of the nasal margin of the left disc. The urine was examined six times, and albumen found, the last of these occasions being on March 27, but when it was examined on March 31 there was no albumen : the specific gravity varied from 1006 to 1015 : granular and hyaline casts were present in the urine. Vomiting remained a feature for the first ten days in the hospital, and during this period the temperature was normal or very little raised. On March 23 herpes developed on the lips and nose, from which there spread on to the nose and cheeks a most severe cellulitis : the eruption occurred even on the tongue : the eyelids became almost closed, the temperature rose to 100°·6 and remained up until the patient succumbed on April 4 to septicæmia.

P.M. Report.—There is some œdema of the legs. The body weighs 6 st. 8 lb. ; there is extensive ulceration of the face. The heart weighs 11 oz., the walls of the left ventricle are thickened, the mitral valve admits two fingers, the tricuspid three : there are vegetations on the cusps of the mitral valve and on its chordæ tendineæ : the aortic and pulmonary valves and coronary arteries are normal : the cavity of the left ventricle is slightly dilated, the other cavities are normal. There is some fluid in the peritoneal cavity. The kidneys weigh 3 oz. each, they are small, the capsule strips with some difficulty, leaving a finely granular surface : the cortex is very narrow, the renal arteries are normal. There are several submucous hæmorrhages in the stomach wall, and similar changes are seen in the intestinal mucosa almost as far as the ileo-cæcal valve. There is slight atheroma at the commencement of the aorta : the abdominal aorta shows a few scattered fatty patches : the brachial arteries are very slightly thickened : the cerebral vessels are normal. There are some patches of exudation in the right retina.

CHART 31.

P.M. Diagnosis. — Chronic Interstitial Nephritis. Facial Cellulitis and Acute Mitral Endocarditis.

Microscopical Examination. — (Kidney injected.)

Summary. — Chronic glomerulo-tubular nephritis.

Details.—The capsule of the kidney is thickened. The cortex measures 4 to 6 mm. With the exception of 1 or 2 per cent. all the Malpighian corpuscles show marked disease. This varies in degree. In some there is swelling and proliferation of the capsular epithelium : in others this occurs with partial obliteration of the capsule : in others the capsule is completely obliterated and the nucleation of the tuft is reduced : in others the corpuscle is completely shrunken and destroyed. There is marked shrinking of the tubules throughout the cortex, isolated tubules, however, being dilated and mostly containing hyaline casts. The shrunken tubules have in many places simply atrophic epithelium, but in many the protoplasm of the epithelium is abundant or fairly abundant, though granular. Throughout almost the whole cortex, between the dilated as well as between the atrophic tubules, there is a well-marked fibrosis, and lymphocytic exudate is abundant and fairly diffuse. The arciform arteries show a trifling thickening independent of spasm (I : I+M = 1 : 5), and intimal fibrosis not due to "crinkling." The same changes are met with in the interlobular arteries, and are in places somewhat more marked.

CASE 32.—C. H., porter, æt. 62, ward 8, bed 22. Admitted for the first time March 2, 1908. Discharged April 8, 1908. Register No. 585.

Symptoms.—The patient was admitted having noticed that he was very tired on getting up in the morning, for two years. Headache had been present a month, and he had been passing water more frequently than usual for a fortnight : his sight had begun

to fail two years previously. He had had scarlet fever twenty years previously, and his nose bled freely as a boy: he neither took alcohol nor smoked.

Physical Signs.—He was a well-nourished man, had a healthy complexion, and looked quite well. The brachial artery was tortuous. The M.I. could not be felt, and the size of the heart could not be sharply defined because of the emphysema present: the heart sounds were indistinct: the aortic second sound was accentuated; an occasional early diastolic aortic murmur was heard. There was no dropsy. Examination of the right eye showed that the disc was rather hyperæmic and swollen and the edge was blurred: there were a few patches of albuminuric retinitis scattered about: the left fundus showed similar features, but more markedly, and the patches were chiefly near the macula. The headache disappeared, but nausea and giddiness occurred.

On March 16, whilst sitting up in bed to have his dinner, he suddenly became unconscious: the pulse could hardly be counted, and he was very cyanosed: he remained unconscious for half an hour, and then gradually recovered (note great fall in blood-pressure). On the evening of the same day he had a second similar attack.

Gradually the symptoms improved so much during the next three weeks that he was allowed to leave the hospital. The temperature was normal or subnormal, except on two days, on March 13 and 20, when it reached 99° and a little over. The urine was examined twenty times, and albumen was always found as a trace to $\frac{1}{7}$th: blood was not present: hyaline and granular casts were found in the urine.

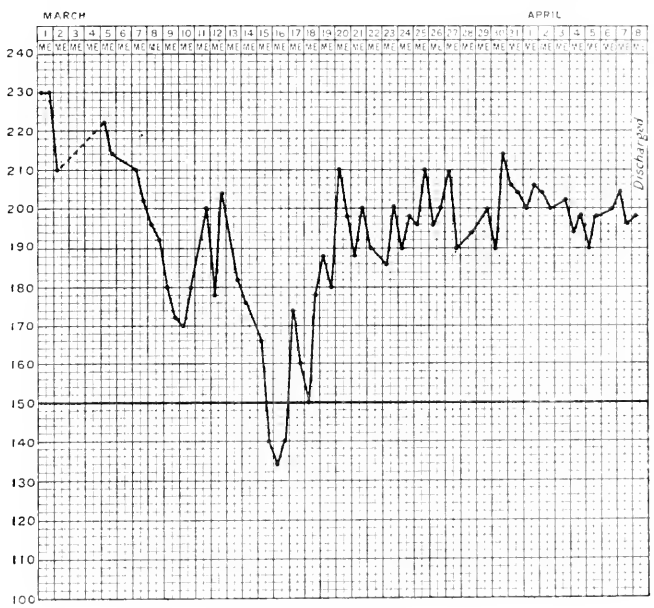


CHART 32.

Second Admission.—He was admitted three years later for the second time on April 14, 1911. Died April 15, 1911. Ward 6, bed 18. Register No. 1191. P.M. Register No. 72.

Symptoms.—The patient was readmitted because he had been found slightly dazed lying on the stairs of his home four days before admission, and said he had had one of his faints, and missed a step: headache supervened: some discharge from his left ear was observed the day before admission. The amount of urine he had been passing had been much reduced for a few days. He had been rather constipated lately, and usually he had been in the habit of passing a large amount of urine, getting up four times at night.

Physical Signs.—He was a well-nourished man: he complained of headache, but was quite sensible. He was able to recollect the names of the nurses who had attended him when in the hospital three years previously: one observation on the blood-pressure registered 234 mm. There was œdema present. He had a feeling of drowsiness. The reflexes were normal. Ophthalmoscopic examination was somewhat perfunctory: there was moderate papill-œdema with exudation at the macula of the right eye. The aortic and pulmonary second sounds were accentuated, the aortic more than the pulmonary: there was a slight tailing off of the aortic second sound: the pulse was not

water-hammer in type. The brachial, radial and temporal arteries were tortuous. At 10 p.m. on the day of admission he was found to be delirious : by midnight he was restless, groaned a great deal, and was apparently unconscious. The left pupil was larger than the right, and reacted sluggishly to light. He was venesected, but there was little improvement in the restlessness : 36 oz. of urine were drawn off, having a specific gravity of 1025 ; there was a very marked cloud of albumen and no sugar. The temperature was 98°·4 on admission ; but the following morning was 104°. At 4 a.m. on the following morning he was deeply comatose. The breathing was stertorous and of the Biot type. There was general muscular relaxation. Lumbar puncture had been performed and the fluid was found to be turbid, but not under great pressure, and organisms were found in the fluid : the patient died of meningitis at 8.30 the same morning.

P.M. Report.—Diffuse purulent meningitis is present, and there is acute otitis media. There is much fat, and the body weighs 11 st. 8 lb. The right kidney weighs 9 oz., the capsule is not very adherent but the consistence is increased, the surface is granular and cysts are seen : the left kidney is small and weighs 3 oz., the surface is smooth and numerous small cysts are seen : the left renal artery is thrombosed from its origin to the division into its branches : the clot is of old standing and organised. The heart is dilated, and there is slight hypertrophy of the left ventricle : weight 19 oz. : the aortic valves are incompetent, the other valves are normal : there are no vegetations. There is atheroma of the aorta, and there is thickening of the coronary arteries. The funduses show retinal hæmorrhages and papillitis. The cerebral arteries show marked atheroma.

P.M. Diagnosis.—Acute Otitis Media, Purulent Meningitis, Thrombosis of the left Renal Artery (old) ; Right Granular (?) Kidney.

Microscopical Examination.—(R. kidney injected.)

Larger Kidney (*right*).

Summary.—Chronic tubular (slightly glomerular) nephritis.

Details.—Capsule of kidney slightly thickened. About 7 per cent. of the Malpighian corpuscles are destroyed—some apparently from a past capsulitis—some doubtful. About 93 per cent. are functional and mostly normal, except for some dilatation of the capsule. The capillaries in some show slight hyaline change, and in a few there is slight proliferation of the capsular epithelium.

There are a few small areas of tubular atrophy in the cortex, which measures 8 mm., but the tubules mostly show changes more resembling a parenchymatous nephritis, the epithelium being cloudy and irregular and in places hyaline. Fibrosis is present and is more diffuse than can be accounted for by the glomerular atrophy, and extends in many places among the non-atrophied tubules.

There are collections of lymphocytes in places. The arciform arteries show a trifling thickening independent of spasm (I : I+M = 1 : 3), and intimal fibrosis not due to "crinkling." The smaller arteries generally are healthy, but there is some hyaline change in places.

Smaller Kidney (*left*).

Summary.—Marked arterio-sclerotic atrophy with extreme glomerular destruction, due apparently to a past capsulitis.

Details.—The capsule of the kidney is thickened. Almost 95 per cent. of the Malpighian corpuscles are destroyed or far advanced towards destruction. In a great number of these the capsule shows the unequal thickening of past capsulitis ; many of the tufts are hyaline. The functional corpuscles show some hyaline change in the capillaries and in the fibrous capsule, and the capsular space is wide. There is extreme, almost total, atrophy of the cortical tubules. Hyaline casts of small size are present in many. Fibrosis is practically absent. The cortex measures 3 mm. Lymphocytes are abundant and diffuse.

The walls of the arciform arteries are markedly thickened, independent of spasm (I : I+M = 4 : 8), and there is marked intimal fibrosis, not due to "crinkling." The interlobular arteries show similar changes.

Case 33.—W. K., painter, æt. 38, ward 6, bed 20. Admitted April 3, 1911. Died June 4, 1911. Register No. 1071. P.M. Register No. 102.

Symptoms.—The patient was admitted with a history of having had pain over the stomach area and shortness of breath for six weeks, and a cough for a month. He had a very bad appetite and constipation, and had had swelling of the legs for a week. The epigastric pain was sufficiently severe to disturb sleep. He was in the habit of getting up once or twice in the night to pass water.

Physical Signs.—He was a well-nourished man, whose breath was very short; he was obliged to sit up in bed. The mucous membranes were pale, and there was œdema about the feet and ankles extending up the legs to a little above the knees. The impulse of the heart was diffuse over the third, fourth and fifth spaces, and the M.I. was forcible and placed in the fifth space in the nipple line: the aortic second sound

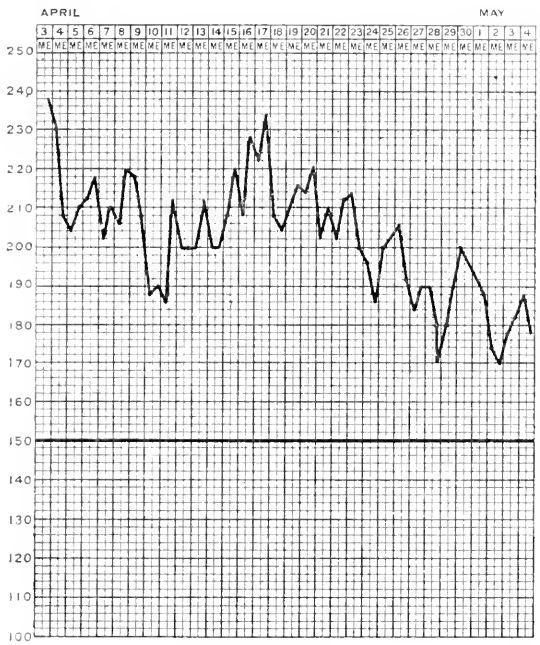


Chart 33.

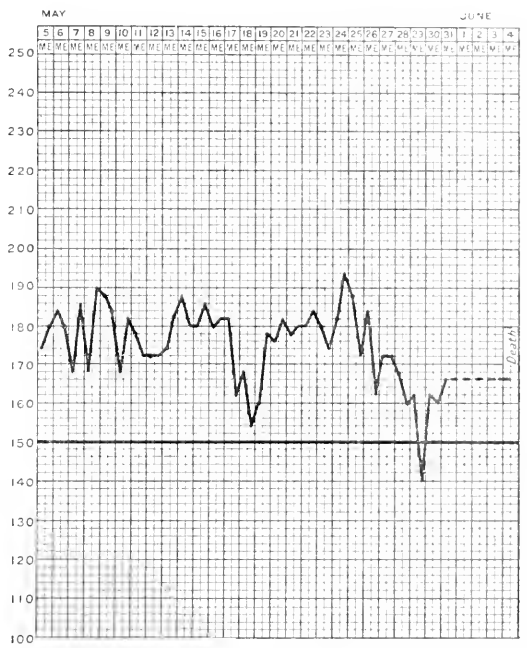


Chart 33 (continued).

was accentuated; the radial, brachial and temporal arteries were thickened and tortuous. There were sonorous and sibilant rhonchi and râles heard in the lungs, the latter especially at the bases. Examination of the eyes revealed a blurred margin of both discs, especially the left, with some swelling of each disc, and patches of exudation in both funduses, with an attempt at an early formation of a star figure at the macula: the arteries showed "silver wire" features and the veins were full, and pressure was shown where the arteries crossed them. Casts were looked for on two separate occasions, and none found. The urine was examined on thirty-five occasions, and albumen found each time: no blood was found: the specific gravity varied from 1010 to 1020. The temperature was generally normal or subnormal; but for twenty days out of the total of sixty-two days that were spent in the hospital there was a rise to about 99°, and once to 101°.

Headache was a very marked feature during his stay in the hospital. His breathing became more difficult and gasping, he rolled in bed and tossed his arms about. He had delusions, hearing voices of imaginary persons. Pericardial friction sounds developed. Fluid developed in both sides of the chest and had to be withdrawn, and the dropsy in his legs increased to such an extent that Southey's tubes were inserted.

Ultimately pleural friction sounds were heard, and a few hours before death coma supervened.

P.M. Report.—Body not weighed. Petechiæ are present in the upper limbs, and the lower limbs are œdematous. The pericardium is covered with recent lymph: the heart weighs 21 oz.; the right auricle is dilated, the tricuspid orifice admits five fingers, the valves are opaque at their edges: the right ventricle is dilated and its wall hypertrophied: the mitral valves admit three fingers, and the valves are opaque at their edges: the left ventricle wall is hypertrophied, but the cavity not dilated, and the aortic valves are normal and competent. The walls of the coronary arteries are thickened: there is early atheroma at the lower end of the aorta. There is recent fibrinous exudation on the pleuræ and some fluid exudation present in the cavities: pneumonia is present in both lungs. The kidneys weigh $3\frac{1}{2}$ oz. each, the capsule is more adherent than normal, the surface finely granular: the cortex is reduced and defined: one cyst is present on the surface: the arteries are a little thickened. The arteries of the brain are a little thickened: there is no atheroma present. The funduses of the eyes show white patches, and one shows some hæmorrhage.

P.M. Diagnosis.—Granular Kidney, Cardiac Hypertrophy, Pneumonia, Pleurisy and Pericarditis.

Microscopical Examination.—(Kidney injected.)

Summary.—Marked glomerular atrophy, probably due to past capsulitis. Consequent marked tubular atrophy. Moderate arterio-sclerosis, probably independent of the former.

Details.—The capsule of the kidney is slightly thickened. About 60 per cent. of the Malpighian corpuscles are destroyed—the shrunken corpuscles show necrotic tufts with unequally thickened and hyaline capsules. About 40 per cent. are functional. Some of these show slight cloudy swelling and proliferation of the capsular epithelium, in a few there is partial adhesion of the capsule and in some slight hyaline change in the tuft.

There is a thick network of tracts of atrophic tubules in the cortex, with intervening islands of dilated and functional tubules. Fibrosis is well marked, and in some places extends in among the functional tubules. In the atrophic areas also, in places, the tubes have the character of chronic parenchymatous nephritis rather than simple atrophy, but this change is relatively slight. The cortex measures 3·5 mm. Lymphocytic exudate is marked in places. The arteriæ arciformes show a moderately thickened middle coat, not due to spasm (I : I+M = 1 : 4), and have a slight intimal fibrosis, not due to "crinkling." The same change occurs in the interlobular arteries, where the intimal thickening is rather more marked. In one arteriole the deposit is very cellular, suggesting syphilis.

Case 34.—J. R., bootmaker, æt. 55, ward 6, bed 16. Admitted July 15, 1911. Died July 22, 1911. Register No. 2275. P.M. Register No. 137.

Symptoms.—The patient was admitted semi-conscious, and the history was obtained from his sister that for some time his neighbours had noticed he had changed mentally. Ten days before admission he began to complain of headache. He became unconscious three days before admission, and had had incontinence of urine ever since the headaches began. He had taken an excess of alcohol, and had had rheumatic fever twenty years previously.

Physical Signs.—On admission he was restless, it was with great difficulty he could be made to answer questions, and his answers were not sensible. The only abnormality found in the nervous system was the affection of consciousness, the incontinence and the impossibility of obtaining the abdominal reflexes: all other reflexes were normal.

The M.I. was rather heaving in character, and internal to the left nipple line: there were no murmurs, nor was the aortic second accentuated. The brachial arteries were not tortuous. There was slight blurring and swelling of the right optic disc, the upper edge especially being ill-defined, the veins were a little tortuous. The

urine was examined on four occasions, and there was no albumen found on one, but a trace or slight trace on the other three occasions: casts were looked for and none found. Some slight twitching of the right arm was noticed occasionally. The degree of consciousness varied, and he died comatose. Shortly before death Cheyne-Stokes breathing developed: knee-jerk was obtainable on the left side, but absent on the right two days before death; but both plantar responses were flexor. The temperature was normal until the last forty-eight hours of life, when it rose to 101° and the pulse rose from 72 to 120. There was no dropsy.

P.M. Report.—The body is well nourished and weighs 11 st. 9 lb. There are about 5 oz. of old brownish breaking-down blood clot in the meninges on the left side of the brain, extending from the tempero-sphenoidal lobe to the occipital lobe and towards the vertex, to within 1 inch of the longitudinal fissure: the hemisphere is flattened: no place of origin for the hæmorrhage can be discovered, the cerebral vessels are uniformly dilated and the walls thickened. The heart weighs 15 oz., there is slight hypertrophy of the left ventricle, the valves and orifices are normal. The kidneys weigh 7 oz. each: there are adhesions of the capsule (scars ?) at the lower poles; the capsule strips off with a little difficulty over the rest of the kidneys where the surface is smooth, the cortex is of normal size, is pale and soft, and occasionally cysts can be seen. The arteries of the body generally show numerous atheromatous patches free from calcification, the mesenteric vessels are not thickened.

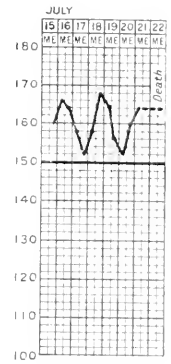


CHART 34.

P.M. Diagnosis.—Left Meningeal Hæmorrhage. Bronchopneumonia, Renal Fibrosis.

Microscopical Examination.—(Kidney not injected.)

Summary.—Chronic parenchymatous nephritis, early or of slight intensity, mainly tubular. Very slight glomerulo-tubular atrophy from past capsulitis. Arterial disease slight.

Details.—Capsule wanting. About 4 per cent. of the Malpighian corpuscles are destroyed, apparently by a past and healed capsulitis. About 96 per cent. are functional, the capsule is very little dilated, the capsular epithelium proliferated in one or two, the fibrous capsule slightly thickened in most, and the capillaries showing slight hyaline change. The tubules have their epithelium markedly swollen, cloudy and granular. Here and there, in a few places, are very small patches of tubular atrophy, with slight fibrosis. In addition to these small scattered areas of fibrosis there is fairly evenly diffused through almost the whole cortex a slight intertubular fibrosis. Lymphocytes are practically absent. There is much congestion. Cortex, 5·5 mm. The arciform arteries show moderate thickening of their middle coats not due to spasm (I : I+M = 2 : 6), with slight intimal sclerosis, not due to "crinkling." The interlobular arteries are less affected.

CASE 35.—A. B., omnibus conductor, formerly a painter, æt. 29, ward 6, bed 2. Admitted October 26, 1910. Discharged November 20, 1910. Register No. 3185.

Symptoms.—The patient was admitted with a history of pain in the "small of the back," swollen legs and face, and shortness of breath for two months previously. He had been "out of sorts" for three months, during which time also, towards the end of the day, the ankles had begun to swell.

Physical Signs.—He was a well-nourished man, his skin was somewhat yellow, and the face showed marked pigmentation on the forehead and temples. There was slight puffiness of the eyelids and œdema of the legs and ankles. The M.I. was visible in the fifth space in the left nipple line and forcible, and there was a systolic murmur at the apex of the heart: there were no murmurs at the base of the heart: the second sounds were accentuated. On November 2 violent headaches began, and although the patient became more œdematous, he still passed as much as 60 oz. of water per diem. Lumbar puncture did not seem to relieve the headache, and on November 3

he became unconscious, had a fit, and bit his tongue. Another convulsion followed soon after, and artificial respiration had to be performed. On November 5 his condition was much improved, and remaining so he was eventually discharged. There were no changes in the funduses of the eyes. There was no report on the condition of the brachial artery. The urine was examined for albumen seven times, and albumen found on every occasion, as well as blood. Epithelial and granular casts were also found. The temperature was variable for the first two days, on two occasions reaching 99° and 100°·4: it remained normal for seven days and then steadily rose again, reaching 101°.

Second Admission.—Admitted, æt. 30 years, October 12, 1911. Died October 18, 1911. Ward 6, bed 23. Register No. 3250. P.M. Register No. 194.

Symptoms.—After the lapse of nearly a year from his first admission the patient was readmitted, saying that he had felt dazed and giddy for the three previous weeks, and during the same time had been short of breath, and swelling of the legs and puffiness of the eyelids had come on. All these symptoms had increased during the five days preceding admission. His appetite had been "poor," and he had had pains in the lower part of his back: there had been no headaches: he had noticed that he had

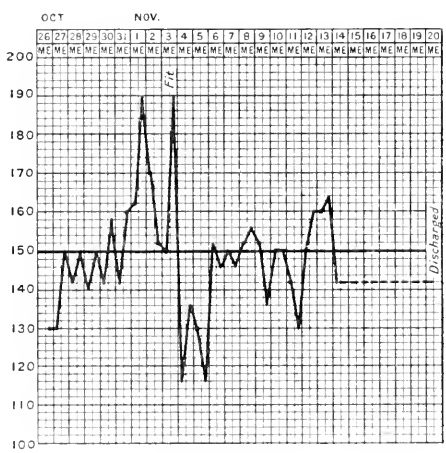


CHART 35A.

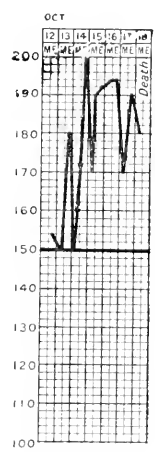


CHART 35B.

at night to pass water two or three times, and it was smoky in appearance. His father had died of Bright's disease. The patient was a total abstainer. Occasionally he smoked a cigarette.

Physical Signs.—The patient was anæmic and the eyelids were œdematous. There was much pigmentation on the upper part of his face and the neck. There was œdema of the hands, wrists, sacrum, feet, ankles and backs of thighs. He was very drowsy, and the breathing was slow, deep, laboured and periodic. The vessels of the neck pulsated up to the angles of the jaws. The M.I. was visible and localised in the fifth space: it was forcible: there was a soft systolic murmur heard at the apex of the heart: the aortic second sound was not accentuated. The brachial artery did not appear to be thickened or tortuous. A retinal hæmorrhage was visible in the left fundus oculi, and the disc looked a little œdematous: there was also a large hæmorrhage in the right fundus oculi: both eyes were normal one month previously when examined in the Out-Patient Department. The temperature for the first three days was subnormal or normal, and the pulse numbered 60 to 80; but in the last twenty-four hours of life the temperature rose to 99°·2 and the pulse to 120 and 136. The urine was examined once: it was smoky, due to the presence of blood, and there was an abundant cloud of albumen. Uræmia gradually increased in spite of hot air baths and venesection, and death ensued in coma.

P.M. Reports.—The body weighs 9 st. : the heart weighs 14 oz. The heart is slightly hypertrophied, the right ventricle especially is dilated : there is slight atheroma of the mitral and aortic valves, but the aorta is normal : both sets of valves function normally. There is some consolidation at the base of the right lung. The kidneys weigh respectively, the right 7 oz., and the left 6 oz. : they are of normal size : the capsule is not thickened, but strips less readily than normal, the surface is smooth and very pale : on section the cortex is slightly reduced : some of the renal arterioles stand out more distinctly than normally : the consistence of the kidney is increased slightly : there are no cysts.

P.M. Diagnosis.—Chronic Parenchymatous Nephritis. Pneumonia.

Microscopical Examination.—(Kidney injected.)

Summary.—Chronic glomerulo-tubular nephritis. Trifling arterial disease.

Details.—Very slight thickening of capsule of kidney. About 10 per cent. of the Malpighian corpuscles are destroyed as the result of capsulitis. About 90 per cent. show capsulitis in varying degrees. In some there is merely some proliferation of capsular epithelium, in others this is extreme. In some, the capsule shows partial adhesions, in others it is almost or quite obliterated, and the tuft is in process of atrophy. In many of the tufts there is slight capillary hyaline, and in nearly all, the fibrous capsules are thickened. Small areas of atrophic tubules occur here and there, but the bulk of the tubules are merely reduced in size, the epithelium remaining granular, though smaller than normal. Almost throughout the whole cortex there is intertubular fibrosis, fairly even in degree. Lymphocytic collections are present in places. The cortex measures 5 to 6 mm. The arciform arteries are only slightly thickened by intimal sclerosis : no spasm or "crinkling" (I : I+M = 1 : 4), and the interlobular arteries show a similar slight change.

Case 36.—C. H., painter, æt. 63, ward 6, bed 18. Admitted January 2, 1912. Died January 20, 1912. Register No. 13. P.M. Register No. 17.

Symptoms.—The patient was admitted with a history of shortness of breath for the previous twelve months. This prevented sleep : he also had had palpitation, pain over the heart, and swelling of the legs during the same period. He had coughed up blood on from twenty to thirty occasions, as much as a teaspoonful at a time : this commenced a month prior to admission, and lasted for a fortnight. He had had gout twenty years ago.

Physical Signs.—The man was well nourished, and lay propped up in bed, suffering from great dyspnœa. There was consideraable cyanosis of the face. There was œdema of both legs and the lower part of the body. The M.I. was in the sixth space, 1 inch external to the left nipple line : it was heaving in character : the heart was also enlarged to the right : two murmurs were heard at the aortic cartilage, systolic and diastolic. The brachial arteries were tortuous and the pulse was collapsing in type. There was considerable emphysema : rhonchi were heard on both sides, and there was impairment of percussion note at both bases. The edge of the liver could just be felt a finger and a half's breadth below the right costal margin, and the upper margin of the liver reached the fifth rib in the right nipple line. Some ascites was present. Eventually serous fluid was drawn from the chest. No changes were found in the retinæ.

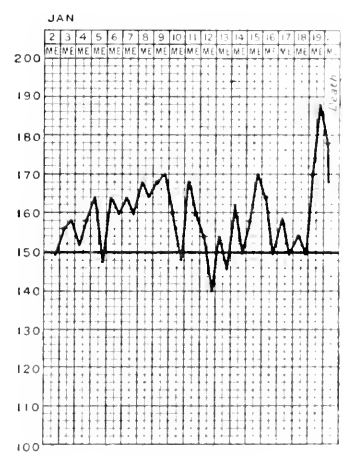


Chart 36.

The temperature was normal throughout the patient's stay in the hospital, except on two days when it reached 99°. The urine was examined nine times, and albumen was found on five occasions and was absent on four : there was no blood, and

the quantity varied from 4500 to 1500 c.c.; the specific gravity was 1010 to 1022. There was no report on casts. On January 20, at 6 a.m., the patient became suddenly very faint and short of breath, and died in a few minutes.

P.M. Report.—Only a partial examination was permitted. The body weighs 8 st. 4 lb., the heart is greatly enlarged and weighs 26 oz. Both sides of the organ are greatly hypertrophied and dilated: the aorta is extensively diseased with atheroma and calcification, it is slightly dilated uniformly, there is very slight atheroma in the sinuses of Valsalva: the segments of the aortic valve are normal, except at their edge, where there is some thickening and calcification: the aortic orifice measures $3\frac{1}{8}$ inches in circumference: the mitral valve is normal, except for slight thickening at the edge of one of the flaps: the orifice admits four fingers, the tricuspid orifice admits five fingers, the coronary orifices are not narrow, but the coronary arteries in their continuity show slight atheroma. The kidneys weigh $5\frac{1}{2}$ oz. each, they are slightly smaller than they should be, the capsule not thickened, is slightly adherent, the surface is finely granular: one cyst is seen on the surface of one organ: the cortex is somewhat reduced in size, the consistence is slightly, if at all, increased. Both lungs are congested: there are no infarctions, or other abnormality.

P.M. Diagnosis.—Chronic Interstitial Nephritis, Hypertrophy of the Heart, Aortic Atheroma.

Microscopical Examination.—(Kidney not injected.)

Summary.—Moderately marked glomerulo-tubular atrophy, probably due to a past and healed capsulitis. Moderate arterio-sclerosis.

Details.—The capsule of the kidney is slightly thickened. About 32 per cent. of the Malpighian corpuscles are destroyed, the destruction being probably due to past capsulitis: the tuft is small and necrotic, and the adherent capsule shows hyaline thickenings: about 68 per cent. are normal, except for slight dilatation of the capsule. Small areas and tracts of atrophied tubules are present in the cortex, accompanied by fibrosis. The functional tubules show epithelium undergoing granular destruction. The cortex measures 5 to 6 mm. Lymphocytes occur in places. The arciform arteries show moderately thickened middle coat not due to spasm (I : I+M = 2 : 5), and the intima moderately sclerosed. The interlobular arteries show the same change, with rather marked tendency to hyaline change.

Case 37.—E. C., widow, æt. 55, ward 14, bed 1. Admitted January 30, 1912. Died February 10, 1912. Register No. 380. P.M. Register No. 34.

Symptoms.—The patient was admitted with the complaint that she had had pains over the heart for six months, with palpitation and shortness of breath for twelve months. She wasted and became weak, and for the two or three weeks before admission her ankles had swollen. Her appetite was very faulty: headaches had occurred occasionally, and recently she had been noticed to "wander."

Physical Signs.—She appeared to be a well-nourished woman, but her complexion was rather sallow. The urine was examined on two occasions, but no albumen was found, and no blood: some granular casts were noticed. There was only slight œdema of the ankles. The M.I. was in the fifth space, internal to the left nipple line: it was forcible in character: there was a systolic murmur at the apex of the heart, and a systolic murmur and an early diastolic murmur at the aortic cartilage, and the second aortic sound was accentuated. There was dullness at the bases of the lungs. There was well-marked albuminuric retinitis, especially in the right eye (exudative type). The brachial arteries were tortuous. Certain symptoms led to pelvic examination and carcinoma cervicis was discovered. The patient became gradually weaker and died eleven days after admission: prior to death left-sided pneumonia developed. The temperature was normal, or about 99° until the end of her illness, when it rose gradually to a maximum of 100°·4.

P.M. Report.—The body weighs 5 st. 9 lb. 4 oz. The heart is hypertrophied and weighs 18 oz., the hypertrophy is more marked in the left ventricle: the mitral valve is thickened and contracted at its free edge: the aortic valve is normal, except for a

thin line of thickening at the attached margin of the cusps: the tricuspid valve is a little thickened, but the orifice is of normal size. The ascending aorta is very slightly diseased, but the rest of the vessel shows diffuse atheromatous change, not very marked, with patches of calcification and small ulcers in two or three places: the aorta is not dilated. There is a large amount of fluid in both pleural cavities. The surface of the consolidated lower lobe of the left lung is covered with hæmorrhagic fibrinous exudate. The kidneys weigh 2½ oz. each, the capsule is thickened and adherent, the surface of the right is finely granular and shows numerous large irregular depressed areas of atrophy of the kidney substance (arterio-sclerotic kidney), the cortex is narrow and the renal artery thickened. There are small white patches of retinitis in the right eye, the left is apparently healthy. There is carcinoma of the cervix.

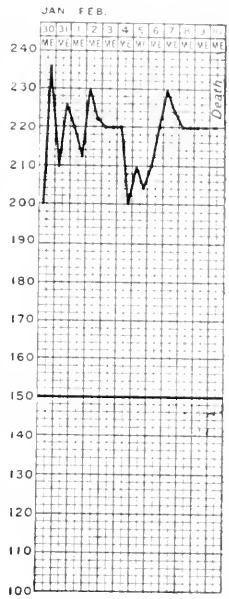


CHART 37.

P.M. Diagnosis.—Mitral Insufficiency, Atheroma, Scarred and Granular Kidneys, Carcinoma Uteri, Pneumonia.

Microscopical Examination.—(Kidney injected.)

Summary.—Moderate to extreme arterial change. Moderate to extreme glomerulo-tubular atrophy, partly arterial, partly capsulitic in origin.

Details.—The capsule of the kidney is thickened. In the greater unscarred part of the kidney the destruction of the Malpighian corpuscles amounts to 13 per cent.; in the scarred portion to nearly 100 per cent. In both cases the corpuscles show capsulitis and atrophied or necrotic tufts, with localised hyaline thickening of the capsule. About 87 per cent. of the corpuscles of the unscarred part are functional: the capsules are slightly dilated, and the capillaries show very slightly hyaline change: in many the fibrous capsule is thickened. In the main part of the kidney the cortex shows a delicate network of atrophic tubules, with fibrosis: the intervening tubules show cloudy swelling and granular destruction of the epithelium. The cortex measures 6 mm. Lymphocytes are few. In the scarred portions of the kidney the tubules are almost all atrophied, and fibrosis is absent.

The arciform arteries in the less altered parts show moderate thickening of the middle coat, not due to spasm (I : I+M = 2 : 5), and intimal sclerosis, and the same condition is met with in the interlobular arteries. Some of the afferent arterioles show a marked hyaline change. In the scarred areas the arterial thickening is extreme, both in the larger and smaller vessels, and in some of the latter the lumina are obliterated: the middle coat is thickened, not due to spasm (I : I+M = 9 : 14); the intima shows extreme thickening, not due to "crinkling."

CASE 38.—F. O., coach painter, æt. 36, ward 6, bed 17. Admitted January 7, 1911. Discharged January 26, 1911. Register No. 76.

Symptoms.—On admission the patient complained of left-sided headaches for two years, and morning sickness for six weeks. He was constipated: he slept well. He gave a history of having had lead colic on four occasions, first time fourteen years ago, and last two years ago: he had also had urethral stricture. He had taken a moderate amount of alcohol, and had had scarlet fever at the age of six years. Vomiting had been frequent all his life: nose-bleeding occurred at the age of thirty-two years. His father died of Bright's disease, and a brother of hæmorrhage into the brain.

Physical Signs.—The patient was a short, spare man who lay comfortably in bed: he was of good colour and showed no tophi. The M.I. was forcible in the fifth space 3 inches from the middle line of the body: the aortic second sound was accentuated. The brachial artery was tortuous. The chest was barrel-shaped, due to emphysema of the lungs. The retinæ were normal; but the arteries pressed on the veins where they crossed them and had a "silver wire" appearance. No casts were found in the

urine after centrifugalisation. The urine was examined sixteen times, and albumen always found: the specific gravity varied from 1011 to 1020: the quantity varied from 30 to 80 oz. The temperature was always normal.

Second Admission.—The second admission took place two years later on January 28, 1913, and he was discharged on February 25, 1913. Ward 8, bed 23. Register No. 325.

Symptoms.—He was readmitted with pain in the lower right side of the abdomen for six weeks, headache and vomiting for three weeks: on one occasion blood was brought up. The pain was centred around an old scar, where he had been operated on for hernia and appendicitis one year and three years previously. His eyesight had been failing for some time.

Physical Signs.—He was a well-nourished man, obviously suffering from pain. His breath was distinctly offensive. The brachial and radial arteries were tortuous. The M.I. was heaving in character, in the fifth space 3 inches from the middle line of the body: there were no murmurs: the aortic second sound was accentuated. Gradually the pain in the

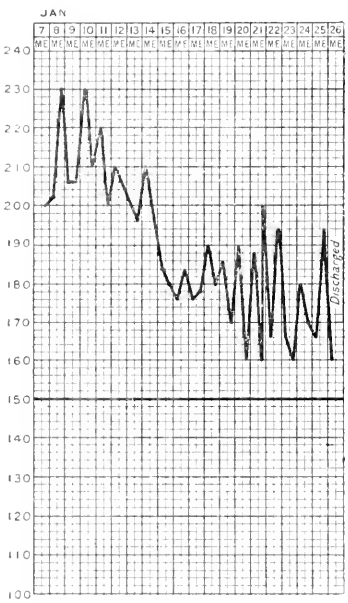


Chart 38a.

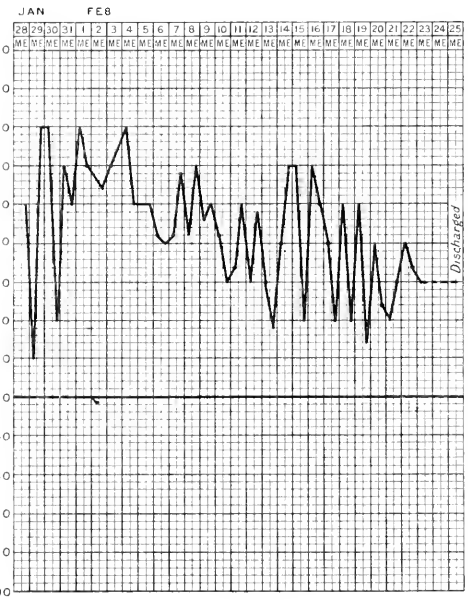


Chart 38b.

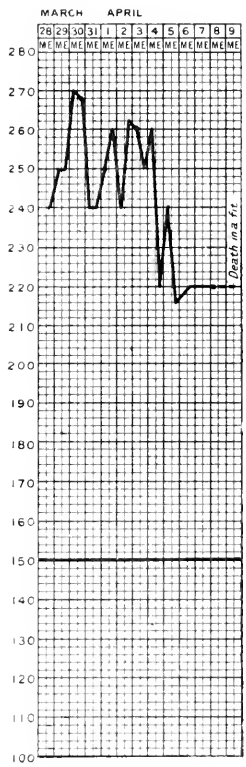


Chart 38c.

abdominal scar disappeared. The arteries of the retinæ were found to be of the "silver wire" type: in the left eye there were two small patches of yellow-white exudate, but no star formation, and no hæmorrhage. The patient steadily improved and was discharged. The urine was examined eleven times, and albumen was always found to be present: epithelial and granular casts were also found on one occasion: blood was always present: the specific gravity, taken seven times, was 1008 four times and 1007 three times: the quantity of water varied from 96 to 30 oz. His temperature was generally normal: on three separate days it reached 99° as a maximum. All the reflexes were exaggerated, but the plantar responses were flexor in type.

Third Admission.—He was readmitted, æt. 38 years, on March 28, 1913, and died on April 9, 1913. Ward 8, bed 13. Register No. 1057. P.M. Register No. 82.

Symptoms.—On this occasion he was admitted because he had had morning

sickness for ten days, and his sight had become very defective for eight days, his sense of colour being lost. The vomiting was associated with diarrhœa. Odd shooting pains about his neck and shoulders were noticed. He had noticed has arms and hands were tremulous lately.

Physical Signs.—The patient was found to be thin and lay comfortably in any position in bed. There was no pallor, cyanosis or shortness of breath, nor was there any dropsy. The breath was very offensive. The temporal arteries were tortuous. The urine was examined on four occasions and albumen was always present: then specific gravity was 1016 to 1020: the quantity varied from 24 to 65 oz.: casts were looked for twice and not seen: blood was found on the last occasion when the urine was examined. Some patches of exudate were found round the disc of the right eye, and there were well-marked "silver wire" arteries: the left fundus was indistinct, but some pale patches of exudation could be seen near the macula: the reactions of the pupils to light and accommodation were defective. The M.I. was heaving in character, was in the fifth space, 3 inches from the middle line of the body: there was enlargement of the heart to the right, the second aortic sound was markedly accentuated: the first sound at the apex was muffled. He was unable to recognise anything held a few feet from his face, and this persisted till death. He became very drowsy, headache and pain in the back continued, and he steadily became worse. Constipation was a great feature. Retention and then incontinence of urine occurred, and the urine had to be drawn off regularly. His speech became rambling and unintelligible, and his respirations of a hissing character, but not periodic: death occurred in a uræmic fit. The temperature for the first four days was normal, or a little above normal, and for the remainder of his stay was subnormal, 96°.

P.M. Report.—The body weighs 6 st. 6 lb. 8 oz. There is no dropsy. The heart weighs 13½ oz., there is hypertrophy of the left ventricle: the valves are normal: the pericardium is normal. The aorta is atheromatous: there is also atheroma of the arteries at the base of the brain. There is a hæmorrhage in the left retina. Each kidney weighs 2 oz., and is red and granular in type: there is thickening of the renal, brachial and radial arteries: the kidneys are small: the cortex is considerably reduced. There were no naked-eye changes in the occipital lobes.

P.M. Diagnosis.—Red Granular Kidneys.

Microscopical Examination.—(Kidney not injected.)

Summary.—Marked arterio-sclerosis, especially of the smaller vessels. Marked glomerulo-tubular atrophy, due largely to the vascular disease, but increased by glomerular destruction due to capsulitis, which is also in progress in most of the corpuscles.

Details.—The capsule of the kidney is slightly thickened. About 37 per cent. of the Malpighian corpuscles are destroyed: in some unequal hyaline thickening of the capsule around the atrophic tuft is present, indicating past capsulitis: in more this is absent and the destruction appears to be due either to hyaline degeneration of the capillaries of the tuft or to anæmic necrosis: about 63 per cent. are still functional, but almost all altered: some show slight proliferation of the epithelium of the slightly dilated capsule: in others there are also adhesions of the capsule: in some the capsule is almost obliterated and commencing atrophy is present in the tuft: in almost all the fibrous capsule is somewhat thickened. The cortex measures 3 to 4 mm., and almost all the tubules are atrophic, only small islands of functional and somewhat dilated tubules being present: the latter contain hyaline casts. Fibrosis is distinct and widespread, and in many parts hyaline. Collections of lymphocytes occur in places. The arteriæ arciformes show moderate thickening of middle coat, not due to spasm (I : I+M = 2 : 5), and moderate intimal sclerosis not due to "crinkling." In the interlobular arteries the change is more marked and has a hyaline character: in many there is great reduction and some obliteration of the lumina, and the proliferation is in many markedly cellular, suggesting syphilis.

Case 39.—E. E., gardener, æt. 42, ward 6, bed 18. Admitted July 22, 1912. Died September 3, 1912. Register No. 2383. P.M. Register No. 163.

Symptoms.—He began to be ill seven months prior to admission with sudden development of shortness of breath. He improved with a month's rest, but on returning to work his symptoms reappeared. Swelling of the feet and body had been present for six weeks. He found that he could not rest at all lying down, but had to be propped up in bed. He had never had headaches: had had to get up at night to pass water for twenty years. So far as he knew he had never had any illness of any kind whatever. He took a pint of beer a day, and whisky occasionally, and smoked 3 or 4 oz. of "shag" a week.

Physical Signs.—He was a well-nourished man, who had to be propped up in bed. There was considerable œdema of the lower extremities and trunk: there was dullness at both bases of the lungs, and bilateral distribution of râles and rhonchi. The M.I. was rather diffuse, situated in the fifth space, not dislocated: a systolic murmur was heard at the apex. The lower border of the liver could be felt below the costal margin, but was not tender: there was ascites. The urine was examined twenty-three times, and a very thick cloud of albumen was found on each occasion, amounting to as much as 2·6 to 4·4 grm. per litre in the twenty-four hours (Esbach): there was no blood, and the specific gravity varied from 1005 to 1020, and the quantity from 400 to 1700 c.c. Casts were looked for on July 23 and 30, and could not be found. The funduses of the eyes were normal at first. The brachial arteries were not reported upon. Friction sounds developed over the precordium on August 15, after incisions had been made over the malleoli to relieve the dropsy on August 7. On August 19 the patient became maniacal. Tremors developed in the hands and occasionally jerky movements. Purpuric patches developed on August 26, and the patient began to waste rapidly. White patches were seen in both eyes, and also a hæmorrhage in the right eye on August 30. The pulse became weaker, the water more scanty, and gradually the patient died uræmic. For the last week before death vomiting was a definite feature. The temperature was normal or slightly raised occasionally for the first seven weeks' stay in the hospital: it was raised to as much as 101° on August 20, subsequent to this the temperature was normal.

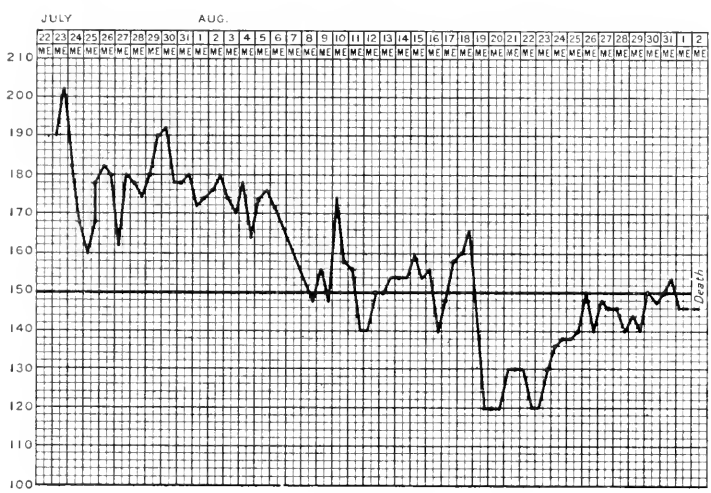


Chart 39.

P.M. Report.—The body weighs 7 st. 1 lb. 8 oz. There is no œdema present. The pericardium shows scattered patches of fibrinous exudate, and there are 3 or 4 oz. of clear fluid in the sac: the heart is enormously enlarged, weighing 21½ oz., all the cavities are dilated and the left ventricle wall is hypertrophied: the tricuspid orifice admits five fingers, and the mitral four, the valves otherwise are normal. The coronary arteries are healthy, the aorta shows a few patches of atheroma. There is a fibrinous exudate on both pleuræ, and a pint of fluid in each cavity. There is a small amount of ascites. The right kidney weighs 4 oz., the left 1 oz.: the latter organ is very much deformed, and shows a dilated pelvis: numerous cysts are seen in it, and the capsule is tough and adherent: the right kidney is small, fairly normal in shape; its capsule is

thickened and adherent, and its surface is granular: there are small cysts present: the substance is very tough. Both ureters are dilated to the size of a little finger. The bladder shows roughening and congestion of the trigone, and contains an oval stone 1 inch in length. The arteries at the base of the brain are normal: there is a small patch of atheroma in one internal carotid artery.

P.M. Diagnosis.—Chronic Interstitial Nephritis, Pericarditis and Pleurisy (Atrophied left Kidney, and Calculus in Bladder).

Microscopical Examination.—(Kidneys not injected.)

Smaller Kidney.—**Summary.**—Probably an early arterial (? syphilitic) disease, leading to congenital deformity and atrophy of the kidney; or calculous atrophy of kidney.

Details.—The capsule of the kidney is thick. Five fairly normal Malpighian corpuscles are present in the section; no others, atrophic or otherwise, are met with. Related to these functional corpuscles are a few islands of normal tubules; elsewhere the tubules are atrophic, many containing small hyaline casts, others dilated or cystic. From the renal pelvis, tubes lined with transitional epithelium branch towards the cortex: these tubes are surrounded with a richly cellular tissue, the cells resembling plasma cells rather than lymphocytes. Lymphocytes are abundant in places. There is no clear line of distinction between cortex and medulla, the cortex measures 0·5 mm. in some places and is absent in others. All the arteries show extremely thickened middle coat, due to spasm or proliferation or both (I : I+M = 4 : 8), and have great intimal sclerosis, in part due to "crinkling" or proliferation, or both: the lumina are often much reduced, and in places obliterated; the new tissue is in places rather cellular, suggesting syphilis.

Larger Kidney.—**Summary.**—Severe arterio-capillary fibrous-hyaline disease. Severe tubular atrophy. Slight capsulitis superadded, with little or no secondary effect.

Details.—The capsule of the kidney is thick. About 70 per cent. of the Malpighian corpuscles are destroyed, the change being mostly due to capillary hyaline changes without reduction in the size of the tuft, and associated with partial or complete adhesions of the capsule. In a few corpuscles there is the ordinary shrinking and atrophy of the tufts. About 30 per cent. of the corpuscles are functional. Some are normal, with dilated capsules: others show commencing hyaline change in the capillaries: others slight proliferation of the capsular epithelium: many have the fibrous capsule slightly thickened. There is very great tubular atrophy, only a few small islands of functional, in places cystic, tubules remaining. Fibrosis is marked, and is very hyaline in parts. The cortex measures 2 to 3 mm. Lymphocytes are present in places. The arciform arteries show a greatly thickened middle coat due to spasm or proliferation or both (I : I+M = 7 : 12), and the intima is much sclerosed, due to "crinkling" or to proliferation or both. The smaller arteries show the same condition, and some of the afferent arterioles are markedly hyaline and narrowed. In places the new tissue is richly cellular, suggesting syphilis.

Case 40.—J. M., skeleton-articulator, æt. 67, ward 6, bed 20. Admitted October 5, 1912. Died October 9, 1912. Register No. 3242. P.M. Register No. 185.

Symptoms.—The patient was admitted with a history of having had shortness of breath on exertion for six weeks, palpitation after effort, and sleeplessness for three weeks. There was slight cough, with some expectoration, and there was a history of getting up at night three times to pass water. His consumption of alcohol was very moderate.

Physical Signs.—On admission the patient was found to be a well-nourished man of normal complexion, who rested propped up in bed showing marked dyspnœa. The pulse was frequent, 112 per minute, regular in force and rhythm. The brachial artery was tortuous. The M.I. was in the fifth space internal to the nipple line: no murmurs were heard: the aortic second sound was accentuated. There was dullness to percussion at both bases of the lungs behind, especially on the right side, where the mi-

paired note reached as high as the spine of the scapula: the vocal fremitus was diminished in this area, and breath sounds weak: rhonchi and râles were heard in the lower part of the lungs on both sides above the dull areas. The urine was examined on four occasions, and albumen was always present, a heavy cloud to a trace: the specific gravity varied from 1032 to 1034, and the amount of urine passed from 200 to 1000 c.c.; granular and epithelial casts were found. On October 6 two pints of clear straw-coloured fluid were drawn off from the right chest, containing a number of white corpuscles of which the majority were lymphocytes; pneumococci were discovered on staining. After the removal of the fluid the breathing became rather easier, but finally assumed the Cheyne Stokes character. The breathing again became more difficult, the sputum purulent, and signs developed indicative of consolidation of the lung at both bases. Œdema had been present in the lower extremities of the lower part of the body throughout his stay in the hospital. The temperature was subnormal on admission, then was normal for two days, reached 101°·6 the day before death, and was again normal on the day of death from pneumonia. The breathing increased from 28 to 36 a minute on admission, to 60 and 58 per minute on the day of death. No report on the retinæ.

P.M. Report.—The body, which is much cyanosed and shows some œdema, weighs 10 st. 13 lb. The heart weighs 22 oz.: all its cavities are dilated and both ventricles hypertrophied, the left very markedly: the tricuspid orifice admits five fingers; the mitral three fingers: the valves of the heart are normal, except that two adjacent segments of the aortic valves are adherent. The coronary arteries are fairly healthy, the muscle substance firm and undegenerated. Three pints of slightly turbid fluid are present in the right pleural cavity, and the surface of the lower lobe of the right lung is covered with a layer of fibrin: at the lower border of the right lung there is a red infarct about 1 inch in diameter: the middle and lower lobes of the right lung show red hepatisation: the lower lobe of the left lung is completely consolidated (red hepatisation). The first part of the aorta shows very little change in the walls: there is slight atheroma in the descending aorta. The liver shows early "nutmeg" change. The right kidney weighs 5½ oz., and the left 6 oz.; the capsules are adherent, not thickened: the surfaces of the kidneys are red and rendered irregular by numerous small angular depressions and pits. There are no cysts present. The cortex is reduced.

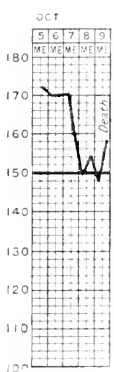


CHART 40.

P.M. Diagnosis.—Cirrhotic Kidneys: Lobar Pneumonia: Infarction of Lung.

Microscopical Examination.—(Kidney injected.)

Summary.—Very trifling glomerulo-tubular atrophy, probably from a past glomerulitis (capsulitis). Cloudy swelling of renal epithelium.

Details.—The capsule is not thickened. About 5 per cent. of the Malpighian corpuscles are atrophied, and in an extreme degree, so that no details can be made out. Most of the corpuscles are fairly normal, except for a slight hyaline condition of the capillaries, some cloudy swelling of the epithelium and dilatation of the capsules.

A few diminutive foci of atrophied tubules are scattered through the cortex. The main bulk of the cortical tubules shows cloudy swelling, with granular destruction. Casts are practically absent. The cortex is 5 to 6 mm. in width.

There is a trifling subendothelial fibrosis in the arciform arteries, not due to "crinkling," the middle coat of the arciform arteries is not thickened (I : I+M = 1 : 3), the interlobular arteries being normal. There is a slight interlobular fibrosis associated with the small areas of atrophic tubules, but none elsewhere.

Lymphocytic exudate is absent.

CASE 41.—W. C., painter, æt. 69, ward 6, bed 20. Admitted October 14, 1912. Died October 23, 1912. Register No. 3336. P.M. Register No. 191.

Prior to admission to University College Hospital this patient had been in the

Brompton Hospital for Consumption and Diseases of the Chest from June 12, 1912, to October 13, 1912. The symptoms and signs during his stay in this latter hospital were the same as those found in University College Hospital.

Symptoms.—The patient had suffered from cough and pains over the heart for eighteen months. For an indefinite time he had suffered also from lumps in the axillæ and groins. Latterly he had become very short of breath on the least effort: sleep was impossible at night unless he was propped up. He had had rheumatic fever at the age of nineteen years.

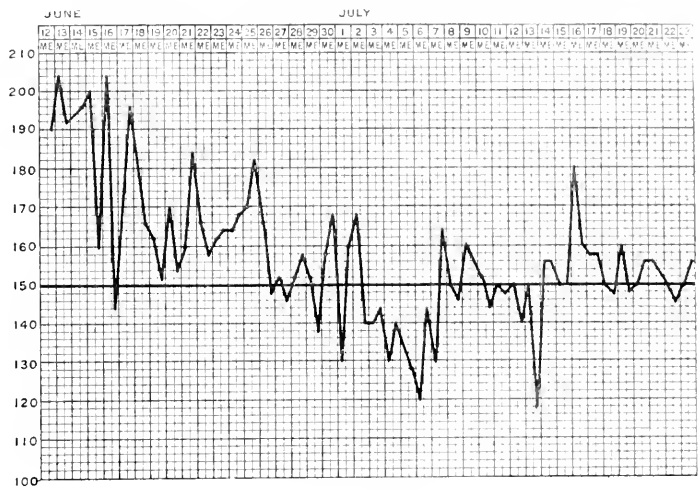


CHART 41.

Physical Signs.—He was a fairly well-nourished man, and was short of breath even when resting propped up in bed. The brachial arteries were tortuous. The M.I. was present in the fifth space internal to the nipple line: there was some increase in the dullness of the heart to the right: a systolic murmur was heard at the apex and another one at the aortic cartilage: the second aortic sound was ringing in character. There was dullness at both bases of the chest behind, reaching up to the inferior scapular angles, and over these areas râles were heard: the breath sounds were diminished, and vocal fremitus was reduced. There was fluid in the abdominal cavity, and the liver was enlarged. There was œdema of the lower part of the body and of the lower extremities. The lymphatic glands were enlarged in the following places: in the posterior triangles of the neck, in both axillæ and in both groins. The spleen also was enlarged. There were marks of incision over the malleoli which had been made on July 27, to relieve the dropsy. Examination of the blood showed that the patient amongst other things was suffering from lymphocythæmia, as lymphocytes numbered 93 to 94 per cent. of the total white cells present, of which there were 420,000 to 770,000 per c.mm. The signs of dullness at the bases increased, especially on the right side, and 25 oz. of turbid fluid were withdrawn, showing the presence of diplococci which were "Gram positive," 72 per cent. of the cells present were lymphocytes, the polymorpho-nuclear cells

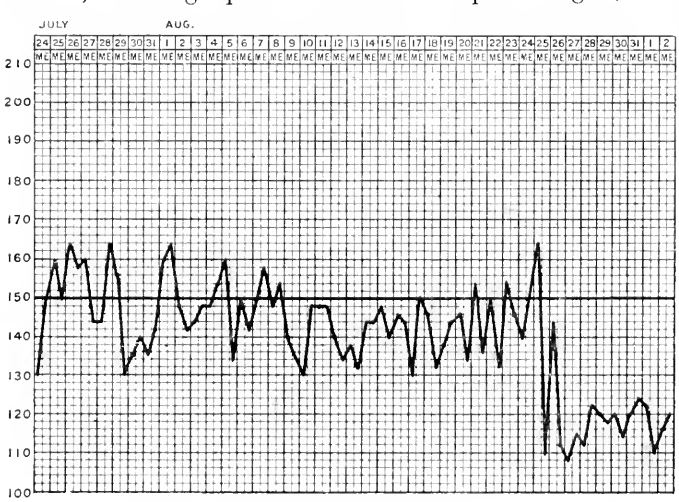


CHART 41 (continued).

numbering 24 per cent. Moist sounds increased in the chest, and inflammatory changes spread from a second more recent set of malleolar incisions. The patient became very restless, and died of septicæmia on October 23. The urine was examined twice and found to contain a slight amount of albumen and a trace. The urine was examined in the Brompton Hospital on fourteen occasions, and showed albumen on eleven, and no albumen on three. There were no changes in the retinæ on June 30, 1912. There was no report on casts. The temperature was normal for the first two days, then rose to 102°, reached normal in four days, remained so for three days, and latterly rose just before death to 100°·4.

P.M. Report.—The body weighs 8 st. 2 lb. It is œdematous. Numerous small subcutaneous abscesses are found in the legs. The deep veins of the leg contain ante-mortem clot. There is no ascites. The heart weighs 15 oz.; the pericardium is normal: there is slight hypertrophy of both ventricles: the right heart is dilated; the aortic valves are stenosed, due to thickening and fusion of the segments: the mitral orifice admits only two fingers. The coronary arteries are atheromatous. The aorta is normal. One and a half pints of clear fluid are present in each pleural cavity. The lungs are

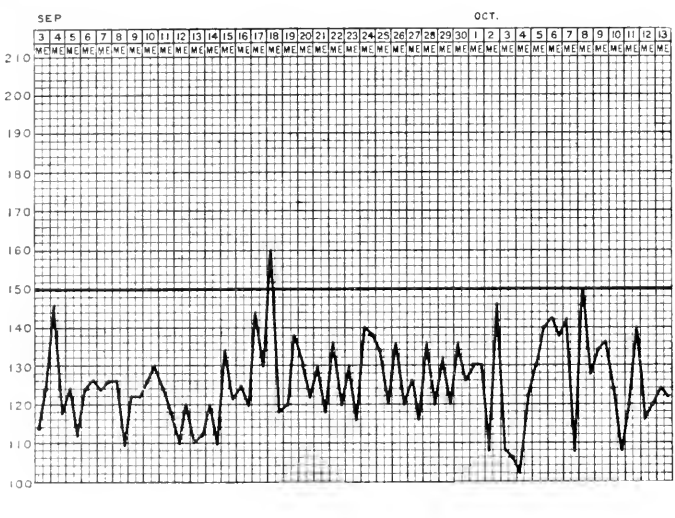


CHART 41 (continued).

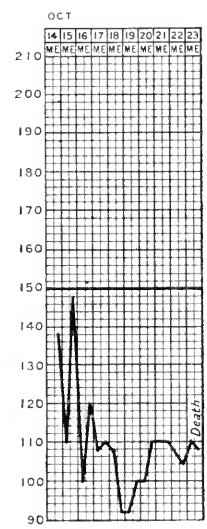


CHART 41 (completed).

hyperæmic and œdematous. The spleen is enlarged, weighing 20 oz. The right kidney weighs $5\frac{1}{2}$ oz., and the left 6 oz.; the surfaces of the kidneys are granular: cysts are present: the cortex is reduced, and the renal arteries thickened. The yellow marrow of the bones is replaced by red marrow. There is general enlargement of the lymphatic glands of the body, which on section are soft and brain-like, but free from hæmorrhages.

P.M. Diagnosis.—Cellulitis of the Legs; Lymphocythæmia, Stenosis of the Aortic and Mitral Valves, Chronic Interstitial Nephritis.

Microscopical Examination.—(Kidney injected.)

Summary.—Slight glomerulo-tubular atrophy, probably due to past capsulitis. Trifling arterial disease.

Details.—The capsule of the kidney is thickened. About 16 per cent. of the Malpighian corpuscles are destroyed, probably as the result of a past capsulitis. Eighty-four per cent. are functional and, except for a little dilatation of the capsule, normal. Small areas of tubular atrophy are scattered through the cortex, fibrosis is associated with these. The main part of the tubules are functional, and show merely swelling or granular destruction of the epithelium. The cortex measures 6 to 8 mm.

Lymphocytes are few in the interstitial tissue, but abnormally abundant in the capillaries (lymphocythæmia). There is very slight intimal sclerosis of the arteriæ arciformes, not due to "crinkling": the middle coat of the arciform arteries is normal (I : I+M = 0 : 1·5). A moderate degree of fibrous-hyaline change is met with in some of the interlobular arteries.

CASE 42.—J. H., police sergeant, æt. 41, ward 6, bed 20. Admitted October 25, 1912. Died November 22, 1912. Register No. 3465. P.M. Register No. 209.

Symptoms.—The patient was admitted with symptoms of pain in the centre of the chest for three months, shortness of breath for two months, and swelling of the feet for five weeks. He had been liable to cough for fifteen years. Sleep was much disturbed. He had at one time of his life been an excessive drinker.

Physical Signs.—He was more comfortable when propped up in bed: but even then was very short of breath. The brachial arteries did not reveal any tortuosity; but there was much subcutaneous fat present which may have obscured this change. The M.I. was felt over a wide area, the centre of which was in the fifth space, 1 inch external to the left nipple line: no murmurs were heard: the aortic second sound could not be heard: there was much emphysema. There was some ascites and dropsy, obvious "bronchitic" signs and some dullness at the right base behind. The urine was examined on nineteen occasions, and albumen was always present: its specific gravity varied from 1010 to 1020: the quantity from 650 to 4250 c.c. in twenty-four hours: casts were looked for on two occasions, and none found. Electro-cardiograms were made, and revealed the fact that the heart muscle was normal in action. The patient vomited on several occasions during his stay in the hospital. Owing to increase of the dyspnœa fluid was drawn off from the right pleural cavity. On October 26 both funduses showed marked albuminuric retinitis, especially the left one, which also showed some small hæmorrhages: there was a commencing "star formation" at the right macular region. Paracentesis of the chest had to be repeated. The bronchitis persisted, and cyanosis became a feature. On November 22 the pulse was noticed to be getting weaker and the patient more feeble: he had been sleeping badly: at 9.45 p.m. he called out suddenly, and without further warning fell back dead. The temperature almost throughout his stay in the hospital was usually normal or subnormal: but shortly after admission there were six days during which the temperature was over 99°, and the last three days of life this recurred.

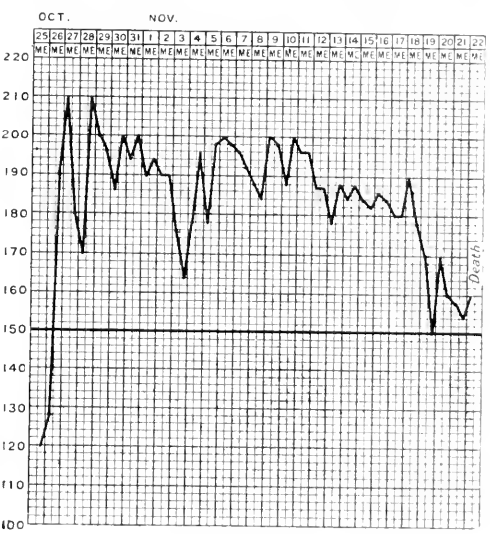


CHART 42.

P.M. Report.—The body is well developed, and there is slight œdema in both lower extremities: it weighs 14 st. 2 lb. The heart weighs 25 oz.: both ventricles are dilated, and their walls hypertrophied: the mitral and tricuspid orifices are dilated: both auricles are dilated and hypertrophied. The coronary arteries are normal: there is a small globular ante-mortem clot softened in the centre and adherent to the lower part of the left ventricular wall: there is very slight atheroma in the aorta. There is turbid fluid to the extent of ½ a pint in each pleural cavity, and evidence of fibrinous exudation on the pleuræ: the lungs show bronchitis and emphysema: five red infarcts are found in the lungs: no emboli found in the pulmonary artery. The liver shows some congestion. The kidneys weigh 9½ oz. each: the capsules are slightly thickened,

not adherent: the surfaces are very finely granular, are purple in colour, and one small cyst is seen: the kidney substance and cortex are normal in width: the consistence is normal: there is no obvious fibrosis: the arteries are slightly more rigid than normal.

P.M. Diagnosis.—Chronic Interstitial Nephritis: Infarction of Lungs: Pleurisy. (At first the kidney was returned as "normal": histological examination and a perusal of the clinical features led to a change of the description!)

Microscopical Examination.—(Kidney injected.)

Summary.—Slight arterio-sclerosis and hyaline change. Slight glomerulo-tubular atrophy, due in part to past capsulitis, in part to arterial disease of smaller vessels.

Details.—Capsule of kidney slightly thickened. About 10 per cent. of the Malpighian corpuscles are destroyed—some from a past capsulitis, others probably from ischæmic atrophy and necrosis. There are small scattered areas of tubular atrophy in the cortex, with fibrosis. The bulk of the tubules show merely granular destruction of the epithelium. The cortex measures 8 to 9 mm. Lymphocytes are scanty. The arciform arteries show slight thickening of the middle coat not due to spasm (I : I+M = 1 : 4) and slight intimal sclerosis, not due to "crinkling," and the interlobular arteries show similar changes. Some of the afferent arteries show rather marked hyaline change.

Case 43.—H. K., bricklayer, æt. 45, ward 6, bed 17. Admitted March 22, 1913. Died March 22, 1913. Register No. 967. P.M. Register No. 60.

Symptoms.—The patient was admitted to hospital having fallen unconscious whilst at work four hours previously. He had not recovered consciousness since the onset, and was comatose on admission. It was only possible to obtain a scanty history from his wife. There was no history of nycturia, of sickness or headache, and no history of symptoms referable to the cardio-pulmonary system. There was no history of recent epistaxis. The patient had had pleurisy seventeen years previously, and the only other departure from health was the occurrence of fits on three occasions—fifteen years ago, four years ago, and five weeks before his present admission to hospital. There were ten children alive, three were dead; his wife had had three miscarriages. The patient had been in the habit of drinking 2 pints of beer and smoking half an ounce of tobacco a day.

Physical Signs.—On examination the patient was found to be well nourished, he was comatose, breathing was stertorous, and his face was flushed. There was squint, which varied from time to time, the pupils reacted to light sluggishly, and were small and equal. The left arm and leg were quite flaccid. Most reflexes examined, including the supinator-, biceps-, knee- and ankle-jerks, were present and equal, but the abdominal reflexes were absent, and the plantar responses were extensor on both sides. On admission the pulse-rate was 48 per minute, and reached 98 later. The blood-pressure, taken on two occasions only, was 256 mm. There was incontinence of urine. A catheter specimen of urine showed a specific gravity of 1020, a very small amount of albumen, and some power of reduction of Fehling's solution: no blood. No reports on casts or on the condition of the retinæ, on the site of the maximum impulse of the heart, or on the condition of the brachial arteries. The temperature was subnormal. The pulse and breathing gradually failed, and the patient died four hours after admission. There was no dropsy present.

P.M. Report.—The body weight was not estimated. The kidneys, which are of normal size, weigh after injection with Müller's solution and formalin, $7\frac{1}{2}$ oz. each: the capsules are not adherent: the stripped surface is smooth: the cortex is a little reduced: there are no cysts: there are numerous minute red points of injection present in the cortex. The heart weighs $17\frac{1}{2}$ oz.; the left ventricular wall is hypertrophied: there is some thickening of the mitral valve: there are some small patches of atheroma near the openings of the coronary arteries: there are only a few small patches of atheroma in the rest of the aorta. There are old pleural adhesions at the base of the right lung: and there are old scars at the apices of both lungs: both lungs are engorged but crepitate throughout: there is no pneumonia.

The left half of the brain is firm : the right hemisphere is much softer and gives the sensation of containing blood within it. Later, on section after hardening, a large blood clot was found in the right internal capsule.

P.M. Diagnosis.—Sclerosis of Kidneys : Cerebral Hæmorrhage.

Microscopical Examination.—(Kidney injected.)

Summary.—Very little beyond cloudy changes. Trifling glomerulo-tubular atrophy, presumably the result of a past capsulitis.

Details.—The capsule is normal. The great majority of the Malpighian corpuscles are normal, except for slight swelling of the capsular epithelium in some, and distension of the capsular space. A few corpuscles (5 per cent.) are atrophied. Most of the tubules show cloudy change in the epithelium, with granular destruction. Casts are absent. The cortex measures 7 mm. A few tubules here and there are atrophied, and in connection with these there is a little fibrosis. Lymphocytes are absent. The arteries show a scarcely recognisable subendothelial thickening, not due to "crinkling" : the middle coat is normal (I : I+M = 0 : 2).

CASE 44.—J. H., æt. 76, ward 6, bed 19. Had given up work for years. Admitted March 7, 1913. Died March 25, 1913. Register No. 813. P.M. Register No. 64.

Symptoms.—The patient was admitted with a history that he had had shortness of breath and cough on and off for ten years. Formerly the shortness of breath was only brought on by exertion, but on admission was continuous and occurred even at rest. He had been in the habit of getting up once at night to pass water. He said he had had gout at the age of thirty-three for the first time, and it continued on and off for thirty-four years. The amount of alcohol consumed was moderate.

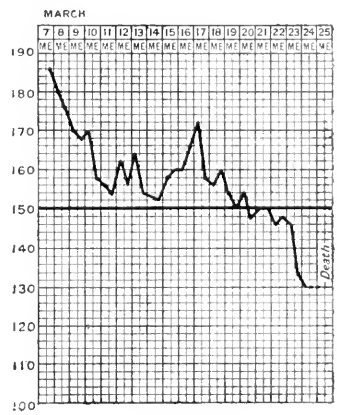


CHART 44.

Physical Signs.—The patient was a feeble old man who, as he lay in bed, was slightly dyspnœic. The legs and lower part of the body were œdematous. There was a large bedsore over the sacrum and petechiæ on the trunk. The pulse was 60 a minute and regular. The brachial artery was tortuous. The M.I. was in the seventh space 6 inches from the middle line of the chest : there was a faint systolic murmur at the apex of the heart : the heart was enlarged to the right. The chest revealed signs of emphysema, and there was dullness at both bases and numerous rhonchi were heard over both lungs. The liver was found to be enlarged ; the spleen was not palpable. The urine was examined on six occasions, and albumen was found five times, and was absent once : its specific gravity varied from 1020 to 1030, and the quantity of urine from 400 to 750 c.c. : granular casts were found on two occasions. Serous fluid was drawn off from the left chest. Gradually the patient sank, dying on March 25, with a temperature of 101°·4, dating from the day previously ; prior to this the temperature had only been 99° on four occasions ; on other occasions it was normal or subnormal. There was no report on the condition of the funduses of the eyes.

P.M. Report.—The body weighs 9 st. 7 lb. The heart weight is 19½ oz. : the pericardium is universally adherent : the left ventricular wall is hypertrophied, the right only slightly; both are dilated : the tricuspid and mitral orifices are dilated, the coronary arteries are atheromatous : the aorta is practically normal : the auricles are a little dilated, the pulmonary and aortic valves normal. Large amounts of fluid are found in the pleural cavities ; the lungs show infarction. The kidneys weigh 7 oz. each, the capsule is thickened and adherent to the kidney, and the exposed surface of the kidney is red and granular and shows embryonic lobulation : the cortex of the kidney is not reduced in width, the consistence of the organ is very tough. Several cysts are present in the cortex.

P.M. Diagnosis.—Chronic Interstitial Nephritis: Coronary Atheroma: Infarction of Lung: Hydro-thorax.

Microscopical Examination.—(Kidney not injected.)

Summary.—Fairly marked glomerulo-tubular atrophy, probably mainly due to a past capsulitis. Slight to moderate arterio-sclerosis.

Details.—The capsule of the kidney is absent. About 36 per cent. of the Malpighian corpuscles are destroyed: the tuft is atrophic and necrotic, and the capsule in many unequally thickened and hyaline, in others only slightly altered. About 64 per cent. of the corpuscles are functional and normal, except for dilatation of the capsules. There is a well-marked but not very coarse network of atrophied tubules in the cortex, with fibrosis. The cortex measures 6 mm. The islands of functional tubules show swelling and granular destruction of the epithelium, and in some, cloudy changes with desquamation. Lymphocytes are scanty. The arciform arteries show moderate thickening of the middle coat not due to spasm (I : I+M = 2 : 5), and intimal sclerosis, not due to "crinkling," becoming less marked or disappearing in the interlobular arteries.

CASE 45.—T. D., æt. 79, ward 6, bed 24. No occupation in recent years. Admitted April 21, 1913. Died April 27, 1913. Register No. 1334. P.M. Register No. 99.

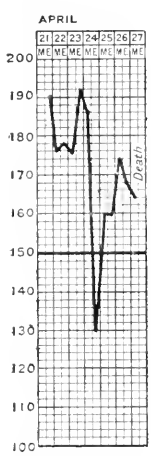


CHART 45.

Symptoms.—The patient was admitted with the complaint that he became short of breath on the least exertion, and had had cough and pain in front of the heart for two months. Swelling of the lower limbs had been present for one month. Palpitation had been an occasional symptom for ten years. He had been accustomed to take four glasses of mild ale a day.

Physical Signs.—He was fairly well nourished, and rested propped up in bed. The face was somewhat cyanosed. The legs and lower part of the body were œdematous. The brachial artery was tortuous. The pulse was irregular. The M.I. was heaving in character and could be seen and felt in the sixth space external to the left nipple line: the heart was enlarged to the right: there was a systolic murmur at the apex of the heart, conducted into the axilla: the second pulmonary sound was reduplicated. Rhonchi were heard on both sides of the chest, more marked on the left side. The liver was enlarged. There was no report on the funduses of the eyes. The urine was examined on four occasions: no albumen was found on one occasion, but was found on three others: no report on casts: the specific gravity varied from 1013 to 1018, and the quantity of urine varied from 900 to 1200 c.c. The temperature was normal or subnormal throughout. Without giving any warning the patient died suddenly on April 27.

P.M. Report.—The body was not weighed. There is marked œdema. The heart weighs 17½ oz., both ventricular walls are hypertrophied, especially the left: the tricuspid orifice admits four, and the mitral two fingers: the right heart is dilated: the left also, but less in degree: the valves are normal, except for slight atheroma at the edge of the aortic and mitral flaps: the coronary arteries are atheromatous, but not narrowed: there is no fibrosis of the cardiac muscle. There is some atheroma throughout the whole aorta except the first part. There is a considerable amount of fluid in the peritoneal cavity, a large collection of clear fluid in the right pleural cavity, and both lungs are congested and œdematous. The liver shows "nutmeg" changes. The right kidney is described as being slightly smaller than normal, weight, 5½ oz., left kidney, 6 oz.: both organs show the capsule thickened and adherent, the surface is finely granular, and there are scattered small cysts: the cortex is not reduced, the substance is firmer than normal: the renal artery is not appreciably thickened.

P.M. Diagnosis.—Chronic Interstitial Nephritis.

Microscopical Examination.—(Kidney injected.)

Summary.—Slight glomerulo-tubular atrophy, probably capsulitic in origin. Slight arterio-sclerosis.

Details.—The capsule of the kidney is thickened. About 3 per cent. of the Malpighian corpuscles are destroyed. Ninety-seven per cent. are functional and normal, except for slight dilatation of the capsule. (In one there is slight proliferation of the capsular epithelium.) Small areas of tubular atrophy with fibrosis are scattered sparsely through the cortex: in the main bulk of the tubules the epithelium is swollen and undergoing granular destruction: in some spots the epithelium shows hyaline degeneration. Capillary congestion is marked. Lymphocytes are few. Cortex, 6 mm. There is slight thickening of the middle coat, not due to spasm (I : I+M = 1 : 4), and intimal sclerosis of the arciform arteries not due to "crinkling"; the interlobular arteries are still less diseased.

Case 46.—W. J., coach-builder (wood-work), æt. 42, ward 6, bed 24. First admission February 10, 1913. Discharged April 19, 1913. Register No. 493.

Symptoms.—The patient was admitted with a history that he had been short of breath for a year, more marked for the last nine weeks, and during this latter period swelling of the body had taken place. On further inquiry it was found that he had

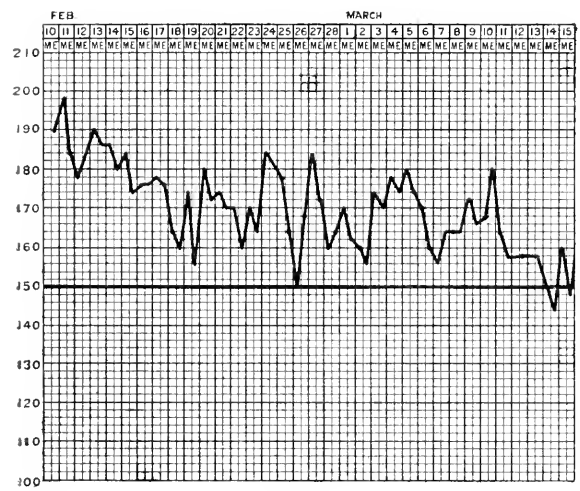


Chart 46a.

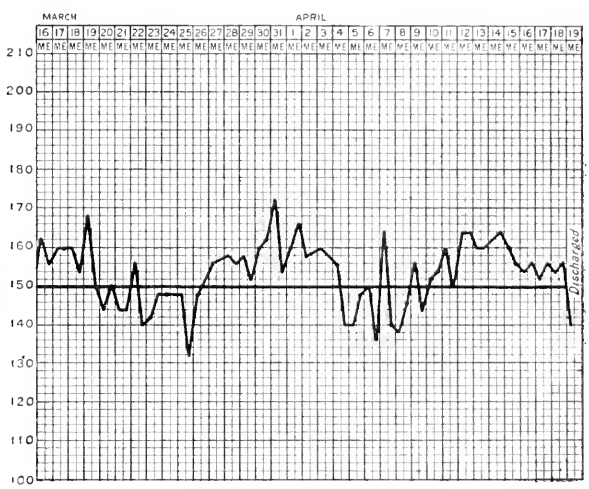


Chart 46a (continued).

had palpitation on and off for a year, and for the same period had been troubled with "night starts," in which he had to sit up in bed and try and get his breath. He had also had cough for eight months, the phlegm was white and frothy, and sometimes streaked with blood. He had been in the habit of getting up at night to pass water for several years. There was a syphilitic history, and treatment had been carried out for fifteen months with mercury. He was an almost complete abstainer from alcohol.

Physical Signs.—The patient was a very stout man, had a healthy complexion, and rested propped up in bed; there was only slight shortness of breath. The pulse was regular in force and rhythm. The brachial arteries could not be seen, as they were obscured by the abundant subcutaneous fat. The M.I. was present in the fifth space 6 inches from the middle line, and subsequently in the left anterior axillary line: the aortic second sound was rather accentuated, and there was a loud systolic murmur at the apex of the heart: no murmurs at the base: the heart was enlarged to the right. Sonorous and sibilant rhonchi were heard all over the chest. There was only moderate swelling of the feet; the abdominal distension was not due to a large amount of ascites, possibly a small amount was present. The liver could be felt 2 inches below the right costal margin. Examination of the funduses of the eyes showed no hæmorrhages or white patches: the arteries had a small degree of "silver-wire" appearance.

By March 5 the small amount of dropsy complained of completely disappeared and the liver projected less below the costal margin. The Wassermann reaction of the blood was positive. The temperature was generally about normal, but on about a dozen occasions was over 99°. Granular casts were present in the urine: the urine was examined on twenty-nine occasions and albumen was always found, from a trace to a cloud: blood was present on seven occasions. The specific gravity varied from 1010 to 1030: the quantity from 500 to 3500 c.c. The patient's condition after ten weeks' stay in the hospital was sufficiently improved for him to be allowed to go home.

Second Admission.—The patient was admitted for the second time on July 29, 1913. Discharged August 15, 1913. Ward 6, bed 24. Register No. 2510.

Symptoms.—The patient was readmitted with symptoms similar to those of his first visit; but with marked pain in the left side of the abdomen, which he had also had on his first visit, but only slightly, and for which no explanation could be found. The output of urine was much reduced.

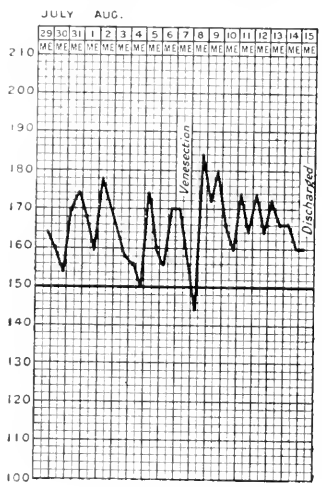


CHART 46B.

Physical Signs.—He had considerable dyspnœa and was somewhat cyanosed. The cardiac condition was as it was on his first admission, with the addition that the pulse had become somewhat irregular and a doubtful presystolic murmur was heard at the apex. Ascites was present to a moderate extent. Widespread œdema of the lungs was present, and there was well-marked swelling of the legs and of the lower part of the body. Granular casts were again present in the urine. The dyspnœa became so great that he was venesected freely on August 7. This gave considerable relief to his symptoms. The liver reached to 1 inch below the umbilicus. The systolic murmur heard on the first visit now became audible once more, as well as the doubtful presystolic murmur. The urine was examined six times, and albumen was always found: its specific gravity varied from 1015 to 1022, the quantity 900 to 2600 c.c. Electro-cardiographic observations of the heart indicated a functional defect of the right branch of the auriculo-ventricular bundle. The patient improved considerably, and was again allowed to return home. The temperature was always normal or subnormal.

Third Admission.—He returned, however, in two weeks, August 28, 1913, in a more urgently serious condition than he was on the two former visits, and died on the same day. Ward 6, bed 10. Register No. 2819. P.M. Register No. 183.

Symptoms.—The patient was readmitted with the history that for the last three days he had passed a very small amount of urine (not more than half a pint), that he had become very breathless, that his eyelids had become puffy, and that there was some swelling of the legs on standing.

Physical Signs.—He was found to be very breathless, and his complexion cyanosed. The cardiac signs were as on the second visit, except that the presystolic murmur was not heard. The brachial arteries were now found to be tortuous, the liver greatly enlarged, and there was ascites. The chest was very emphysematous, but on this admission no adventitious sounds were heard. There was no dropsy in the legs. The urine was examined and albumen was found: no blood. There was no report on casts, or on the examination of the eyes. Temperature was 99°. No observations on the blood-pressure. Death took place quietly, and was associated with marked dyspnœa.

P.M. Report.—The body is well nourished, and there is no œdema: it weighs 11 st. 12 lb.: there are 6 oz. of fluid in the pericardium: no pericarditis. The heart weighs 39 oz.: the walls of both ventricles are hypertrophied and the chambers dilated, the valves are normal: the aortic orifice is not dilated: the coronary arteries are very

little thickened : the aorta shows very slight atheroma. There is slight ascites. The liver weighs 92 oz., slight " nutmeg " changes are present, and some irregular fibrosis : the consistence is tougher than normal. Each kidney weighs 10 oz. : the renal artery is not thickened, the capsule is thickened and not adherent, the surface is smooth and the colour of the organ purple : no cysts are present. The cortex is about normal in width, and the renal arterioles stand out prominently on section.

P.M. Diagnosis.—Large smooth Fibrotic Kidney with Hypertrophy of the Heart.

Microscopical Examination.—(Kidney not injected.)

Summary.—Very trifling glomerulo-tubular atrophy, the result probably of a past capsulitis. Cloudy swelling of epithelium.

Details.—Capsule thickened. About 5 per cent. of the Malpighian corpuscles are destroyed, the tuft shrunken and necrotic, and surrounded by an unequally thickened capsule. Ninety-five per cent. of the corpuscles are normal, except for some dilatation of the capsule. The cortex shows a few narrow tracts of tubular atrophy with fibrosis. The bulk of the tubules have their epithelium swollen or undergoing granular destruction. Cortex, 6 mm. The arciform arteries are practically normal (I : I+M = 0 : 2). There is a slight sclerosis of one or two of the smaller vessels.

CASE 47.—J. R., clerk, æt. 56, ward 6, bed 17. Admitted September 8, 1913. Died October 5, 1913. Register No. 2905. P.M. Register No. 218.

Symptoms.—The patient was admitted with a history of shortness of breath and palpitation, especially marked for the last three weeks, but present for some time previously. He had also noticed that he was wasting. Past illness—rheumatic fever seven years ago.

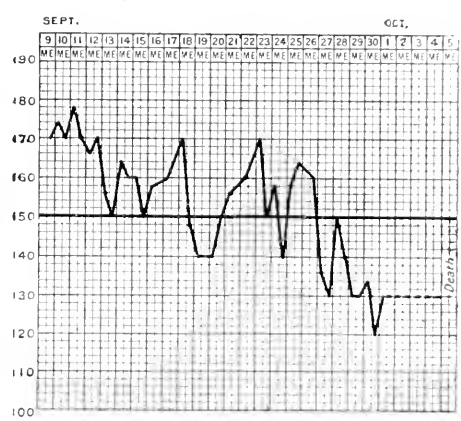


CHART 47.

Physical Signs.—He was a rather emaciated man, who frequently during his stay in the hospital exhibited Cheyne-Stokes breathing. The M.I. was dislocated downwards and outwards about $5\frac{1}{2}$ inches from the middle line, and was heaving in character : the heart was enlarged to the right : there was a "bruit de galop" at the apex, and the aortic second sound was accentuated. The brachial artery was tortuous. There was dullness to percussion at the right base behind, and a few rhonchi at the left base. The liver could be felt four fingers' breadths below the right costal margin : there was no ascites : pericardial friction sounds were heard. There was well-marked œdema of the legs. Sleeplessness and dyspnœa and Cheyne-Stokes breathing continued to be features throughout his illness. Fluid was drawn off from the right chest. Gradually the patient developed some delirium, which, however, improved and passed off. Pleural friction sounds were heard at the left base, and the dropsy, which had improved, returned. The Cheyne-Stokes breathing became very much exaggerated, and the patient gradually became comatose and died. Granular and hyaline casts were found in the urine, and a considerable quantity or a trace of albumen was found on each of the seven occasions on which it was examined : the specific gravity varied from 1020 to 1024 : the quantity varied from 400 to 1250 c.c. The temperature was normal or subnormal except on five occasions, when it was raised above 99°. There was no report on the condition of the eyes.

P.M. Report.—The body weighs 7 st. 1 lb. The heart weighs 20 oz. : both ventricular walls, but especially the left, are hypertrophied and dilated : there is early pericarditis : the coronary arteries are normal. There is fibrinous pleurisy and abundant effusion on both sides of the chest : there is a large hæmorrhagic infarct in the right

lung. The liver is "nutmeg" in appearance. The kidneys weigh 3½ oz. each: they are small, the capsule is thickened and adherent: the cortex is reduced and irregular: the renal arterioles show up as white points: the consistence of the kidney is not increased: the renal artery is slightly thickened. There is slight atheroma of the aorta, and little or no general arterial disease.

P.M. Diagnosis.—Chronic Interstitial Nephritis, Pericarditis, Infarction of Lung, Pleurisy.

Microscopical Examination.—(Kidney not injected.)

Summary.—Marked arterio-sclerosis. Marked glomerulo-tubular atrophy, the result of the arterial disease reinforced by marked capsulitis.

Details.—The capsule of the kidney is thickened. About 60 per cent. of the Malpighian corpuscles are destroyed. These show small atrophic or necrotic tufts, with hyaline change in some, and the contracted capsule showing unequal hyaline thickening: 40 per cent. of the corpuscles are functional; most of them are normal, with slightly dilated capsules; in some the tuft is compressed and rounded and the fibrous capsule thickened; in a few in which atrophy is in progress there is proliferation of the capsular epithelium and partial obliteration of the space. There is a coarse network of atrophic tubules in the cortex, with fibrosis in parts, little or none in other parts. The functional tubules show granular destruction of the renal epithelium. There is intense capillary congestion. Lymphocytes are abundant in places. The cortex measures 3 to 5 mm. The arteriæ arciformes show marked thickening of the middle coat not due to spasm (I : I+M = 4 : 9), with marked intimal sclerosis not due to "crinkling," and narrowing of the lumen. The interlobular arteries are similarly affected, and many have pin-hole lumina.

Case 48.—A. R., formerly a clerk, æt. 70, ward 6, bed 19. Admitted November 2, 1913. Died November 11, 1913. Register No. 3253. P.M. Register No. 247.

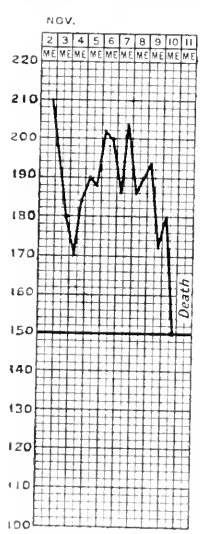


Chart 48.

Symptoms.—The patient was admitted with "burning pains" on both sides of the abdomen, reaching down to the legs, for one month. There had been slight cough and expectoration for two years: for three to four months there had been very frequent and painful micturition day and night, and there was blood in the urine. He had wasted, and nausea and vomiting and sleeplessness had been common symptoms. There was puffiness of the eyelids in the morning and slight headache. There had been no antecedent illness other than measles and whooping-cough.

Physical Signs.—The patient looked healthy and was free from any cyanosis. The M.I. was in the fifth space in the left nipple line, but was not forcible: there was some enlargement of the heart to the right: there were no murmurs nor accentuation of second sounds. The brachial arteries were tortuous. There were signs of diffuse bronchitis and some dullness at both bases. The funduses of the eyes showed no hæmorrhages or white patches, but the vessels revealed a "silver wire" appearance. The urine was examined three times and blood and albumen were present on each occasion: the specific gravity varied from 1012 to 1020, the quantity varied from 300 to 1900 c.c.: casts were looked for but not found. On November 9 tremor of the hands developed, as well as twitching of the arms and forearms, and the patient endeavoured to get out of bed without reason: at other times he was distinctly drowsy. No dropsy of the body or legs. Pain on passing water continued, as on admission. The patient became weaker, and still more drowsy, and finally comatose and died. The temperature had been normal, or subnormal, throughout his stay.

P.M. Report.—The body weighs 8 st. 6 lb. The heart weighs 15 oz. (No other abnormality was reported, except that the coronary arteries were diseased.) There is

much atheroma in the lower part of the aorta. The bladder is greatly distended, its walls are thin, and it contains bloodstained urine: an ulcer 1½ inches in diameter occupies the trigone: the base of the ulcer is formed by a whitish carcinomatous tumour which extends to the middle lobe of the prostate: the ureteral orifices are involved in the growth. The right kidney weighs 3½ oz., it is smaller than normal, the pelvis and calices are much dilated, the kidney substance is much reduced: the ureter is dilated. The left kidney is larger, the capsule is thin; the surface is pale, and mottled with red areas; the pelvis and calices are dilated, the cortex is reduced and tough; a few cysts are present; the ureter is dilated to the thickness of a finger; the kidney weighs 10 oz.

P.M. Diagnosis.—Carcinoma of the Bladder, Secondary Hydronephrosis.

Microscopical Examination.—(Left kidney injected.)

Summary.—Slight hydronephrosis in left, more marked in right kidney. Moderate arterio-sclerosis. Marked glomerulo-tubular atrophy, resulting from these conditions and reinforced by slight capsulitis.

Details.—The capsule of the left kidney is slightly thickened. The papillæ are flattened. About 10 per cent. of the Malpighian corpuscles are destroyed, mostly by a past capsulitis: about 90 per cent. are functional, but most of them show compression of the tuft and some thickening of the fibrous layer of the capsule. There is marked atrophy of the cortical tubules with fibrosis, and many of the functional tubules are flattened in the direction of the surface of the kidney. The cortex measures 3·5 mm. Lymphocytes are abundant. Some of the tubules of the papillæ are filled with polymorpho-nuclear cells. The arciform arteries show moderate thickening due to intimal sclerosis, which may in part be due to "crinkling" (I : I+M = 3 : 5). The same conditions are met with in the interlobular arteries, and in them a hyaline tendency becomes rather marked.

Case 49.—E. K., perambulator-maker (nothing to do with paint or lead), æt. 52, ward 6, bed 21. Admitted April 6, 1914. Died May 5, 1914. Register No. 1206. P.M. Register No. 90.

Symptoms.—On admission the patient's chief complaint was that for the previous seven weeks he had suffered from pain in the upper abdomen one hour after food, independent of the nature of the food, whether solid or liquid. For three to four weeks he had been in the habit of vomiting twice a week, usually after breakfast: although he had never vomited blood, blood had been found in the stools, the last time three months previously. There had been another ill-defined pain in the lower left abdomen on and off for a year. He had noted some distension after meals for the last five weeks, and during the same period he had been very constipated. Amongst other symptoms was some flatulence for two to three years. Shortness of breath, palpitation at night, cough (once or twice traces of blood were brought up) and headache were features for some time past. He had noticed that he was physically weaker, that he slept badly, and was in the habit of getting up to pass water three to four times in the night. There was no history of excessive consumption of alcohol or of excessive smoking: nor was there any history of syphilis.

Physical Signs.—The patient was a spare, sallow-looking subject: the left kidney was palpable. The brachial and temporal arteries were tortuous. The maximum impulse was present in the fifth space, one-quarter of an inch external to the left nipple line: the impulse was forcible, and the aortic second sound was accentuated: a faint early diastolic murmur was heard at the apex of the heart on April 29. Rhonchi were heard on both sides of the chest. The retinæ showed no abnormality, except a little thickening of the arteries. The urine was examined nineteen times and albumen always found: no casts were found in the urine: the specific gravity varied from 1010 to 1015. The temperature was never more than 99°·4, and towards the end of life was subnormal. Slight twitchings developed and the patient became semi-comatose: this deepened to coma, and despite the use of intravenous injections of bicarbonate of soda the condition did not improve, and he died, the blood-pressure having fallen

considerably. The extraction of some very faulty teeth was carried out on April 24, *i.e.* twelve days before death: this was followed by a severe attack of cellulitis of the jaw and face; but the temperature did not rise to more than 99°. The patient, however, shortly after this showed "uræmic" signs such as drowsiness and severe sickness, and the pressure fell from 220 mm., ten days before death, to 140 mm., the last reading, taken two days before death. At death there was slight œdema of both lower extremities.

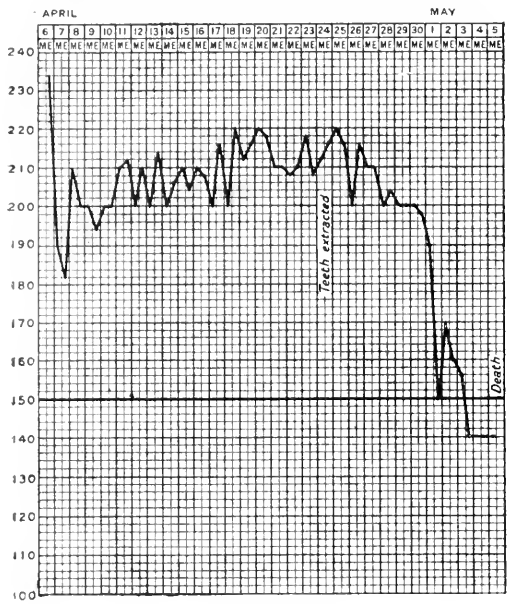


CHART 49.

P.M. Report.—The body weighs 7 st. 12 lb. 8 oz. The heart shows scattered patches of thickened pericardium: weight 21½ oz.: left ventricular wall greatly hypertrophied: slight atheroma of attached margins of aortic valves which are competent when tested with water: aortic orifice not enlarged: mitral valve admits three fingers, tricuspid four fingers: right ventricle dilated, but wall not appreciably hypertrophied. The aorta shows moderate atheroma, increasing in degree at its lower end: the iliac arteries are markedly diseased: most of the arteries of the body are thickened and stiff: this applies to the brachial, posterior tibial, superior mesenteric, splenic and renal arteries. There is marked œdema of both lungs, and there is a thin layer of fibrin on the surface of the left lung. The spleen is small, and not softened. The liver is rather small, but smooth on the surface: not tough: the arteries on the cut surface appear somewhat thickened. The right kidney weighs 4 oz., and the left 4½ oz.: the capsule is slightly thickened, and not adherent: the renal artery is thickened and rigid: the surface is evenly granular, and red: there are several cysts in the cortex: the whole thickness of the kidney substance is reduced, cortex narrowed: the arterioles are somewhat more prominent on section than normal. The brain is normal, and stomach and intestine are free from ulceration.

P.M. Diagnosis.—Red Granular Kidney, Arterio-sclerosis, Cardiac Hypertrophy, Pleurisy. Septicæmia (from cellulitis of face).

Microscopical Examination.—(Kidney injected.)

Summary.—Marked glomerulo-tubular atrophy, originating probably in capsulitis. Moderate arterio-sclerosis of the kidney vessels generally, becoming very marked and hyaline in individual vessels, and probably syphilitic in nature (?).

Details.—The capsule is slightly thickened. About 46 per cent. of the Malpighian corpuscles are atrophic and destroyed. The remainder are functional, but some are slightly altered. In some there is slight swelling of the capsular epithelium, with a little proliferation in one or two; and many of the glomerular tufts are slightly compressed. Large tracts of cortical tubules are atrophied, the atrophy being mostly of the simple kind, but here and there are patches suggesting chronic tubular nephritis, though not of any considerable size. The intervening areas of non-atrophied tubules show little alteration. The cortex measures 4 mm.

The arciform arteries and the interlobular arteries show slight thickening of the middle coat in part due to spasm (I : I+M = 1·5 : 4·5), and slight intimal sclerosis possibly due to "crinkling"; but in places the latter vessels are greatly diseased, the fibro-hyaline change producing much narrowing of the lumen: in some vessels the

lumen is filled with proliferated cells. The capillaries of the glomeruli are slightly hyaline in many cases.

There is some fibrosis around the atrophic tubules in some areas; but it is not marked, and in many places is hardly recognisable.

Lymphocytic exudate is rather abundant.

Brachial artery.—Very trifling subendothelial fibrosis.

Posterior tibial artery.—A rather marked subendothelial fibrosis, and general thickening of the vessel walls: but the artery is contracted.

Liver.—The branches of the hepatic artery in the portal canals are mostly normal: one of them shows a slight subendothelial fibrosis.

Middle cerebral artery.—On one side of the vessel is a very thick subendothelial deposit, very cellular in character and undergoing liquefaction in one part.

Pancreas.—A branch of the splenic artery shows rather marked intimal thickening. In the gland substance most of the arterioles appear normal, one or two are sclerosed. The gland itself shows no change.

Coronary artery of heart.—A branch from the inter-ventricular groove shows very great subendothelial fibrosis and hyaline, with cellular characters marked in places. The small branches in the heart muscle itself are not thickened.

Central artery of optic nerve and branches in retinæ. Normal.

Aorta.—Fibro-hyaline thickening of the inner coat, very marked in some spots. The new tissue is highly vascularised in places, and in its deeper layers is undergoing some liquefactive degeneration. In places the media is involved in the fibrosis.

Ileo-colic artery.—This artery is very thick and resembles a vas-deferens: the lumen measures $\frac{1}{10}$th of the diameter of the vessel. The endothelium is proliferated into two or three layers thick. The adventitia is very dense: both it and the intima are thickened to about an equal degree, and together equal the media in width. The artery is contracted, the lumen taking a stellate form.

Case 50.—W. L., coal and firewood dealer, æt. 50, ward 6, bed 14. Admitted April 23, 1914. Died April 23, 1914. Register No. 1853. P.M. Register No. 107.

Symptoms.—Four hours previous to admission the patient had gone to the lavatory and had an action of the bowels: a few minutes later he was found semi-comatose: then he had several severe attacks of vomiting. When found in the lavatory he knew those about him, but was unable to speak. Within a few more minutes he became quite unconscious, and was admitted to the hospital in that state. The patient was known to be a very irritable man; there was a history of excessive addiction to alcohol—beer, wine and spirits—and he was accustomed to smoke 3 oz. of "shag" a week. According to a brother, the patient had had another paralytic stroke on the right (?) side of the body a month or two previously.

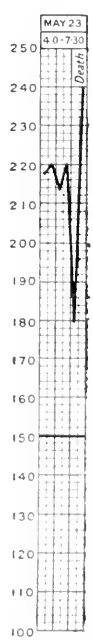


Chart 50.

Physical Signs.—The patient was a burly-looking man, fully ten years older-looking than he really was. He was comatose and the breathing was stertorous: the face was rather pale, and dilated venules were present. Neither pupil reacted to light, the right pupil was slightly larger than the left, both were small. The left arm and leg were flaccid, and there was less tone in the left abdominal muscles: the knee-jerks and Achilles-jerks were equal and very brisk; there was no ankle clonus, and yet the plantar responses were extensor on both sides: the abdominal reflexes were absent. There was incontinence of urine and motions. The brachial artery was tortuous: the M.I. was forcible, and was felt in the fifth space in the left nipple line: both the aortic and pulmonary second sounds were accentuated. The urine was only examined once, and showed a good deal of albumen and a specific gravity of 1014. There was no report on casts or on the funduses of the eyes, but no casts were found in the urine drawn off after

death, and the fundi oculi were normal post-mortem. Lumbar puncture was performed during life, but no relief was given to the condition of coma. The fluid was found to be intimately and uniformly mixed with blood, and it was concluded that the patient was suffering from a right cerebral hæmorrhage. There was no dropsy.

Venesection was also tried, but only 5 oz. of blood were abstracted, and the patient died shortly after. The pulse had risen from 60 to 120, the respiration from 24 to 40, and the temperature from 96°·6 to 101°·2. Several observations were made on the blood-pressure during the short interval he survived in the ward: the highest reading was taken just prior to the cessation of life, namely, 240 mm.: on each occasion it was considerably above normal.

P.M. Report.—The body weight is 8 st. 4 lb. The convolutions of the brain are flattened, especially on the right side: there is a large hæmorrhage in the right centrum ovale: a second in the right side of the pons, and an old focus about 1 inch in diameter in the anterior part of the right occipital lobe: blood is present in the lateral ventricles, very little in the fourth ventricle: the basal arteries of the brain are very little diseased. There are no hæmorrhages or patches of exudation in the funduses of the eyes.

The heart weighs 13½ oz., the left ventricular wall is considerably hypertrophied, the right only slightly: otherwise the heart is normal. The lungs are deeply congested: there are old pleural adhesions in both sides. The spleen is small, soft and deep red in colour: it is slightly adherent to the adjacent structures. The surface of the liver is adherent at nearly all parts to structures around. In several places the capsule shows white patches of perihepatitis ¼ inch thick. The kidneys are small, weighing 4 oz. each: the capsule is thick and adherent: the surface is red and finely and uniformly granular: one or two small cysts are seen: the cortex is not reduced, and the substance tougher than normal: the renal artery is much diseased. The aorta is fairly healthy.

P.M. Diagnosis.—Cerebral Hæmorrhage; Granular Kidney.

Microscopical Examination.—(Kidney injected.)

Summary.—Marked glomerulo-tubular atrophy and destruction. Moderate arterio-sclerosis.

Details.—The capsule is thickened. About 50 per cent. of the Malpighian corpuscles are atrophied and destroyed by capsulitis (?): the rest are fairly normal, except for some distension of the capsule: one or two, however, show some hyaline changes in the tuft, and partial adhesions of the capsule. There is a coarse network of atrophic cortical tubules, the atrophy being extreme and many of the tubules evidently totally destroyed. The cortex measures 4 to 5 mm. The arciform arteries show thickening of the middle coat not due to spasm (I : I+M = 2 : 8), moderate intimal sclerosis not due to "crinkling," and the same degree of change is present in the smaller arteries; only in one or two vessels is there any extreme hyaline or other change. Hyaline change is present in a few of the glomerular tufts, but generally speaking it is absent. There is a good deal of loose fibrous tissue in the atrophic areas, with collections of lymphocytes.

Posterior tibial artery.—Marked arterio-sclerosis, the intima much thickened, and the muscle of the media split up into small islands by tracts of fibrous tissue.

Central artery of retina and its branches.—Normal.

Brachial artery.—Trifling subendothelial thickening.

Middle cerebral artery.—Marked arterio-sclerosis involving the whole wall. The same condition in the arterioles of the adjacent brain substance.

Coronary artery of heart.—Slight subendothelial fibrosis.

Liver.—Some portal fibrosis with thickening of the capsule, but no arterial disease.

SECTION II

ANALYSIS OF THE CLINICAL AND PATHOLOGICAL DETAILS OF FORTY-SEVEN CASES OF HYPERPIESIA

SEX

Men . . .	36	Women [1] . . .	11

WHATEVER each observer may think with regard to hyperpiesis, whether it is merely a physiological peculiarity, or whether it may be exalted to the position of being a sign of a pathological entity, there can be little doubt that there is great difficulty in determining its causation. The above figures show roughly that three-quarters of the cases occur in men, and one quarter in women. Such facts suggest that the more outdoor laborious life of the former plays a part in the causation. This is, however, unlikely, because hyperpiesis occurs in children and in the young adult. A boy æt. 13 years has recently been under observation for albuminuria and hyperpiesis (systolic pressure, 195 mm.) : at death the heart was found to weigh 11 oz. and the kidneys 2 oz. and $2\frac{1}{4}$ oz., and they were granular : this boy had led the most sheltered life, and had been singularly free from the infections of childhood which are liable to cause damage to the kidneys.

OCCUPATION

Painters . . .	9	Cabdrivers and carmen	3
Housewives . .	8	Labourers . . .	3
Domestic servants .	3	Porters . . .	2
		Clerks . . .	2

One case each occurred in connection with the following occupations : cellarman, wood-carver, plumber, stoker, packer, fishmonger, house-agent, bootmaker, gardener, skeleton articulator, police-sergeant, bricklayer, coach-builder (woodwork), perambulator maker, coal and wood merchant, and two cases occurred in old men who had not worked for years.

Hyperpiesis has been considered to be intimately associated with disease of the kidneys : indeed, by some it is considered to connote kidney disease. The frequency with which painters are affected with sclerosis of the kidney would cause little astonishment to such authorities when painters head the list in this

[1] Three cases (all women), namely : Nos. 18, 21 and 27 during life were thought to be cases of Hyperpiesia ; post-mortem examination showed this view was wrong, as the heart in each did not show characteristic hypertrophy. The hyperpiesis observed, such as it was, was an expression of intracranial hæmorrhage in two cases (18 and 21), and of nervousness and excitement in Case 27.

series; but when it is observed that housewives show an almost equal number, it is evident that some other cause must be found. A considerable number of other occupations were those which required severe muscular effort: but in only two other categories were there as many cases as in the class "domestic servants"; and though it is admitted that such women carry out much muscular work in their day's duties, yet their labour can hardly be compared with that of carmen and labourers. The number of porters affected was two, and the number of clerks was two. It does not seem from these figures that the position is established that laborious occupations are the causes of hyperpiesis.

AGE AT DEATH.

		Per cent.
20 years to 29,	3	6
30 ,, 39,	6	12
40 ,, 49,	16	32
50 ,, 59,	10	20
60 ,, 69,	8	16
70 ,, 79,	4	8

Hyperpiesis is alleged to be a function of age, and that for each year after puberty 1 mm. of pressure may be added to 100 mm. to express what is the normal pressure for the given age. Such a view is erroneous, because it is well known that elderly men who are still vigorous, and in every way healthy, may show a systolic blood-pressure constantly below 150 mm. A normal young adult has a systolic blood-pressure of 120 to 130 mm.: experiment on the cadaver shows that the stiff arteries of patients who have died, and who previous to death had had hyperpiesis, are capable of "absorbing" as much as 20 to 30 mm. of pressure as read by the sphygmomanometer: for this reason 150 mm. has been taken in this investigation as the upper limit of normal blood-pressure: there is no doubt that a persistent systolic blood-pressure of 140 to 150 mm. in an adult who has normal arteries would indicate hyperpiesis; but as it is impossible clinically to be sure that the arterial wall is normal, the above raised "threshold" has been adopted in this study.

The largest number of deaths occurred between 40 and 49 years of age—a period when great demands are made upon mankind, both physically and mentally: these factors may help to determine the high mortality at this period.

It must be noted that this list of deaths does not indicate that, given a number of people all of whom have had hyperpiesis *all* their lives, there is an increasing and decreasing change in the mortality-rate culminating between 40 and 49 years. It merely indicates that more cases of hyperpiesis were admitted to the hospital and died between the ages of 40 and 49 years than at other ages: the reason for this may be quite independent of any greater susceptibility to hyperpiesis or to death from Hyperpiesia at that age. It is probable that the causes underlying Hyperpiesia operating upon members of the leisured classes would develop its more serious effects at a later age.[1]

[1] See Discussion on Hypertension, *Transactions of the Assurance Medical Society*, 1917, p. 188.

ALCOHOLISM

A definite history of addiction to alcohol was admitted in ten cases, and in the remaining thirty-seven it was either absent or not admitted. In view of the fact that frank admissions of alcoholic habits may not be forthcoming, a clear deduction cannot be made from these figures : but knowledge of each individual case of the series had shown repeatedly and conclusively that well-marked hyperpiesis occurred in women or men who were, and always had been, teetotalers.

There is a very widespread belief that addiction to alcohol, especially amongst those whose lives are strenuous ones, is a potent factor in the production of hyperpiesis. The pharmacology of alcohol is directly opposed to this view, and so far as clinical study is concerned cirrhosis of the liver dependent upon addiction to alcohol is not accompanied by hyperpiesis. It is conceivable that the excessive consumption of alcohol is either a mere accompaniment, or even is an effect of the causes underlying hyperpiesis. At any rate, as the above figures show, the alcoholism is not so widespread amongst cases of hyperpiesis as is generally supposed. The impetus given by the belief that the " alcohol " habit causes hyperpiesis has probably led to closer observation for this sign amongst this class of patient.

PREVIOUS HISTORY OF KIDNEY DISEASE

This was admitted in only eight cases. In the remaining cases there was no admission, or there was no record of the disease having occurred. As will be seen later on, granular kidney was found post-mortem in about 50 per cent. of the cases. It is quite in conformity with clinical experience that cases of granular kidney in the early stages only quite exceptionally give evidence of kidney disease. Granular kidneys declare themselves not in their early, but in their later stages of development : as a rule, this development is slow.

DURATION OF SYMPTOMS

The intervals which elapsed between the onset of symptoms and death were as follows :

One year or less	29
Two years or more than one year	8
Three years or more than two years	2
Four years or more than three years	2

Among those of rather long duration may be mentioned two of five years, one of eight years, one of ten years, one "a very long time," and one of nineteen years. This study unfortunately could not include an observation on the number of years that the patients had suffered from hyperpiesis ; but in one at least of the cases it was observed at intervals for two years (No. 6). Observers of hyperpiesis are able to state from their experience that they have known the sign to exist continuously for as many as eighteen years, in one case the observations having been made by means of some form of sphygmomanometer.

Observations on hyperpiesis, based upon digital examination only, are unreliable : during the course of these observations different observers of varying degrees of skill gave extremely erroneous answers, on more than one occasion the least experienced observer proving to be nearer the truth than the most experienced (*sic*)

It is freely admitted that the finger may in certain cases detect that there is hyperpiesis, particularly in those cases where the radial artery is large and the subcutaneous tissues are not abundant. The fact remains, however, that the finger is quite unable to detect without fail all examples of hyperpiesis. If the radial artery is small or obscured by adjacent fat, then the finger proves itself to be a most unreliable instrument. The routine instrumental examination of the blood-pressure of all patients admitted to the wards has shown itself to be of the greatest clinical assistance.

SYMPTOMS

No attempt has been made to analyse the frequency of each individual symptom. The symptoms have been grouped according to whether they indicated involvement of this, that or other system, *e.g.*, under renal symptoms are included headache, sickness, polyuria, foul breath (?), etc. Under cardiac symptoms are included dyspnœa on effort, dropsy, palpitation, etc. Under gastro-intestinal symptoms are included hæmatemesis, vomiting, dyspepsia, diarrhœa, etc. Under vascular symptoms are included epistaxis, petechiæ, blindness from retinal hæmorrhages, etc. Under respiratory symptoms are included hæmoptysis, cough, various forms of expectoration, etc., and under nervous symptoms are included convulsions, apoplexy, blindness independent of retinal change, coma, stupor, etc.

In some of the cases there were symptoms referable to more than one system, and as such they have been recorded.

Renal symptoms .	32	Vascular . .	8
Cardiac . .	34	Respiratory . .	8
Gastro-intestinal .	12	Nervous . .	21

A glance at these figures shows with what reason some workers would prefer to speak of cases of Hyperpiesia as cardio-renal or reno-cardiac disease : but it is hoped the study will show that this would be a mistake, as these latter terms indicate merely the peculiar expression these cases show of the underlying cause of hyperpiesis.

A further point must be referred to, and that is the well-known one that hyperpiesis may be present, and be completely dissociated from any symptoms of any kind, or even signs, and may be only discovered when a catastrophe like apoplexy occurs in a patient who was previously quite well, apparently, at any rate, so far as the patient was aware, for he or she so frequently stated that health had been perfect except for this, that or other symptom thought to be due to increase of age.

The reader cannot fail to be impressed with the similarity of the various

symptoms and signs accompanying the hyperpiesis, with those which constitute the manifestations of what is known as "uræmia." Just as it may be said that the detection in the urine of proteins has helped the clinician to a more correct understanding of various "uræmic" manifestations which do not point directly to renal disease, so too, and indeed even to a greater degree, has the discovery of raised blood-pressure done the same. The writer has known a patient whose sole symptoms were those of extreme neurasthenia: indeed the patient was, when seen, undergoing treatment for neurasthenia: there was no albuminuria, but the systolic blood-pressure was found to be 240 mm., and this led to the more guarded opinion that possibly the extreme mental and bodily fatigue was not so much an exhaustion-neurosis as the direct result of the severe toxæmia underlying the hyperpiesis: the patient died within two days, having developed Cheyne-Stokes breathing and coma.

Experience has shown that considerable numbers of persons showing hyperpiesis are entirely free from symptoms. It is true that leading questions may reveal the fact that slight effort causes inordinate dyspnœa, or that the patient could not sleep on the left side, owing to the disturbance of sleep by the violent action of the heart. There can be little doubt, too, that the occurrence of râles and of rhonchi leads too often to the diagnosis of "bronchitis," even though the expectoration is apparently only mucoid; such cases are frequently due to œdema of the lung, which is a common sign of Hyperpiesia.

SIGNS

Hyperpiesis

As already stated, hyperpiesis was present in each case. Special reference will be made to those charts which are more or less representative. The chart of Case 1 will be seen to show many readings below 150 mm., and yet at the post-mortem of the case, as in each of the others, the heart was found to be characteristically hypertrophied. It has been urged by various writers that single occasional observations on hyperpiesis may be most deceptive. This study shows how cogent is this criticism, and Chart 1 enables the reader especially to appreciate the criticism. It will be seen that the systolic blood-pressure had been taken every hour instead of only night and morning. A single observation at 3 p.m., on April 21, would have shown undoubted hyperpiesis, and yet if the only observation had been made at 4 a.m., on April 23, the blood-pressure would have been found to be normal. Even if observations had been made at 9 a.m. and 9 p.m., but slender evidence of hyperpiesis would have been obtained, because only at 9 p.m. on April 21, at 9 a.m. on April 22, at 9 p.m. on April 23, and shortly before death on the morning of April 24, did the systolic pressure rise above 150 mm., and then not to a large amount. The same remarks apply to clinical temperature charts: it frequently happens that the state of infection is reflected by a temperature chart of quite modest degree, and it is well known that severe infection accompanied by the most obvious evidence of severe inflammation may

be unaccompanied by any rise of temperature whatever. With but slight rise of the temperature above 99° and of the systolic blood-pressure above 150 mm. taken on several occasions, there is equal cause for the suspicion of infection in the one as of Hyperpiesia in the other. The reader is reminded that this is a study of cases showing a rise of blood-pressure above 150 mm. and of the results found at the post-mortem examination: in this case, as in others, the modest rise of pressure was found to be associated with the post-mortem evidence of characteristic cardiac hypertrophy.

The chart of Case 2 is typical of a number of other cases. There are two separate sets of observation: in the first record, the blood-pressure was always above 190, and in a great proportion of the observations above 220 mm. during the six weeks of observation. Between April 10 and 16 a great fall of the blood-pressure was observed, and this ultimately was followed by a resumption of the original high level. Such temporary falls of blood-pressure are frequent, and it is difficult to say to what cause to attribute them. They may mean temporary relaxation of arterial spasm, or they may mean temporary weakening of the cardiac over-efficiency: yet again they may mean the occurrence of both phenomena. Why such temporary changes in the work of the arteries and heart should occur is one of the problems which must be settled in the future. The theory is an attractive one, that the change is due to falling off and resumption of effectiveness in whatever agency is responsible for the hyperpiesis. It may be said at once that this particular effect was not due to any therapeutic agent. Mere rest in bed could not be held to be responsible, because despite the continuation of rest the pressure rose again to its former level. On several occasions it has been found that such falls of pressure have been due to temporary infections: if these were remedied, then the original level of hyperpiesis was resumed: if the infection was severe and "terminal," then it frequently happened that the blood-pressure fell and remained low, falling so much that the pulse could no longer be felt—a common occurrence just before death. The second part of the chart was not such a complete record as the first part: a constant level of the hyperpiesis was not maintained; sudden and unexpected death occurred, no readings having been taken for several previous days.

Two separate readings were taken in Case 3, representing the different admissions to the hospital—the first beginning in November and the second beginning in January, more than two years later. The first record shows what is not an infrequent occurrence, when cases of hyperpiesis are given complete physical and mental rest. In less than a fortnight the pressure from being well marked subsided to the normal; dropsy also disappeared and the patient was allowed to leave the hospital. The only frequently effective therapeutic measure used in this and other cases was physical rest: no medicinal measures ever secured so effective and such marked results. These cases are comparable with those of "postural" or "orthostatic" functional albuminuria. The comparison is, however, limited; for though a return to the upright posture in home life led to the reappearance of the hyperpiesis as shown in the second record, death from

syncope and fits, associated with acute pericarditis, occurred on January 11, and hyperpiesis on this occasion, as in Case 1, persisted, although the patient was in bed, to within a few moments of death. Most of the symptoms which were present during the first admission to hospital of Case 3 abated with the fall of pressure, and whatever was the cause of the hyperpiesis was apparently the cause of the accompanying symptoms: with the return of the hyperpiesis the symptoms, especially the headache, returned. It is quite clear, however, that the degree of hyperpiesis is not necessarily a measure of the severity of the accompanying symptoms. It frequently happened that the symptoms lessened during observation, although the hyperpiesis in several cases was maintained, and commonly the hyperpiesis lessened in other cases, although the symptoms were still persistent. This, again, is analogous with what occurs in fever. It is common knowledge that elevated temperature may occur and yet the patient may have little or no symptoms: commonly slighter fever may be accompanied by many and severe symptoms, and it is arguable that just as fever and its accompanying reactions may not be parallel, varying with the cause of the fever and the peculiarity of the patient, so, too, there may be several causes of hyperpiesis with quite different degrees of blood-pressure and collateral symptoms, and the effect may vary with the same cause of hyperpiesis acting on differently constituted individuals.

The chart of Case 4 shows with what marked rapidity the blood-pressure may fall from 224 mm. until it was so low (between 70 and 80 mm.) as to lead to loss of the pulse. In about sixty hours the blood-pressure fell through about 150 mm. In this particular case it is possible that the cause of the fall of blood-pressure was infection, as shown by petechiæ, symptoms of gastro-enteritis, and signs of pleurisy during life, and at the post-mortem pericarditis, pleurisy and broncho-pneumonia. Death was immediately ushered in by delirium followed by a fit. Throughout the patient's stay in the hospital fever was always absent. It is thus seen in this case, as in others (see Chart 51, p. 166) that the blood-pressure chart actually gave warning of the occurrence of infection when the thermometer and pulse failed to do so. As to the relationship of the fit to the fall of the blood-pressure, it must be stated that the fall is in no way regularly accompanied by convulsions, not even when the low pressure has rather quickly, as in this case, replaced high blood-pressure.

The chart of Case 5 shows that up to the moment of death the blood-pressure was raised to as much as 200 mm.: death was said to have taken place from uræmia, as the patient just before death had become restless and showed "hissing" breathing. The temperature a few days before death had risen to 102° in the axilla, probably from erysipelas. In this case the occurrence of the infection had not been sufficient to cause a fall of blood-pressure, at any rate not until the actual moment of death; but it is more than probable that it was the actual cause of death, though uræmia was assigned as the cause. Case 6 shows two charts taken at different times during the same year: a false sense of security was given by the second one, as the rest in the hospital appeared to lead to the fall of the blood-

pressure: in less than two months after his discharge in January 1910 the patient had a severe cerebral hæmorrhage, and the blood-pressure was found to be higher than on any former occasion, namely, 245 mm. It has been found experimentally that increase of intracranial pressure will cause a rise of blood-pressure, and no doubt the cerebral hæmorrhage had contributed its share of pressure effect, accounting for the extremely high blood-pressure found on the fifth and final admission to hospital. Venesection had apparently led to a fall to 204 mm.

TYPES OF CHARTS

It will be seen that the forms of the charts are various in the extreme, but that it is possible to differentiate some well-marked types.

1. *Plateau charts.*—In this group the hyperpiesis is maintained at a fairly high level, and with a moderate degree of daily remission. Good examples are seen in Charts 5, 6A, 24, 25 and 37. A variant of the group shows, instead of moderate remissions, very considerable ones, the curve passing through falls or rises of as much as 50 mm. in the course of a day or two or three days (see Charts 14, 17 and 20A). The cases showing "plateau" charts may be further divided as follows:

(*a*) Cases in whom, despite the persistence of a plateau chart, the symptoms markedly abated, *e.g.* Charts 2A, 6A, 7A, 32, 35A and 46B. It was found that despite the high blood-pressure the patients were able to get up and be about the wards, and eventually were discharged to their own homes, and in several cases a considerable time elapsed before they were readmitted with a return of symptoms.

(*b*) Other cases maintained a high level of blood-pressure to within a few hours of death, or even to within a few moments of death. The latter cases were usually those in whom death was finally brought about by cerebral hæmorrhage (see Charts 6, 34, 43 and 50). But quite a number of cases occurred in whom death took place with the blood-pressure maintained at a high level within a few hours of the exitus, independent of cerebral hæmorrhage, see Charts 2, 5, 9, 14, 17, 24, 25, 29B, 32, 34, 35B, 36, 37, 38C, 39, 40, 42, 45, 48 and 49. Of these cases several died of terminal infections such as pneumonia, pleurisy, empyema, erysipelas, etc., *e.g.* Cases 5, 9, 14, 25, 32, 34, 35B, 39, 40, 42 and 49. Case 37 died of carcinoma cervicis, and Case 48 of carcinoma of the bladder. The remainder of these cases died of the undetermined condition of uræmia: Case 34 died of meningeal hæmorrhage and of pneumonia.

2. *Charts showing falling pressure.*—This group is a large one, because the fall of the blood-pressure was frequently met with not only in those who improved and lost their symptoms, at any rate for a time, but it was a common phenomenon in those of the series of cases whose death occurred at the end of a period of progressive increase of symptoms. The group may be divided into four types, according to the degree of fall of pressure and according to the rate of fall, as follows:

(*a*) Cases in whom the fall of pressure was limited or large. Improvement occurred with a mere *lowering* of the blood-pressure, as seen in Charts 6B, 20A,

29A, 38A, 38B, or with a fall of the blood-pressure to *normal*, as seen in Charts 3A, 22A, 26A, 46A.

(*b*) In this subdivision—a large one—the intensification of the illness, accompanied by a fall in the blood-pressure to normal, appeared to be due to the onset of some infective process, such as pneumonia, pericarditis, pleurisy with or without effusion, empyema, etc. Sometimes evidence of these infections was discovered before death: indeed it soon came to be recognised that if the patient appeared to be getting worse and the blood-pressure was falling, whether fever occurred or not, a routine examination for an inflammatory complication should be regularly made. Petechiæ were found repeatedly, also indicating the occurrence of such inflammation. In other cases the evidence of the existence of these terminal infections was only forthcoming at the post-mortem examination. The charts exemplifying this condition are 3B, 4, 7B, 10, 13, 14, 15, 16, 19, 20B, 22B, 23, 24, 25, 26B, 28, 31, 33, 39, 40, 41, 42, 44, 47 and 49. Charts 30 and 48 show falls associated with these terminal complications, but in addition cancer of the stomach occurred in the former case and cancer of the bladder in the latter.

(*c*) It will be further seen that some of the charts show that the pressure has not only fallen moderately or to normal, but has actually fallen to a subnormal level. This is seen in Charts 4, 7B, 12, 13, 15, 16, 19, 20B, 21 and 41. Terminal infection again played a large part, and was so severe as to cause subnormal pressure.

(*d*) The fourth and last type of this group includes those cases in whom the lowering of the blood-pressure was sudden, that is, occurring in two to four days, as in the Charts 4, 7B, 12, 16, 28, 40, 42 and 48. So striking is the amount of fall in a short time, and so prone is the patient to have severe symptoms during this period, that they deserve to be sharply defined as by the use of such a term as "hyperpiesic" or "hypopiesic crises."

Occasionally it happens, as is seen in Chart 7A, that the fall in the blood-pressure may be only temporary, and the chart subsequently shows maintained hyperpiesis.

3. *Charts showing a further increase of blood-pressure.*—This phenomenon is not so common as is the fall of blood-pressure. What is noticed is that quite independent of any therapeutic measures, or of any excitement, the pressure gradually rises, the patient in the meantime having been kept at rest in bed. This is seen in Charts 20A and 28B, the rise of pressure being maintained in the latter case for over a fortnight.

Cases 24 and 26 actually show a wave-line configuration of chart, with increasing and falling blood-pressure. The occurrence in conditions of complete rest of rises and falls of blood-pressure during several days is of importance, indicating as it does changes in the cardio-vascular system which are of a temporary, as opposed to a permanent, character. The interpretation of this phenomenon will be discussed later.

Charts 2A, 10 and 32 show that hyperpiesic crises may be extremely abrupt, producing rapid falls and rises: extreme forms of crises are seen in Charts 12, 29B, 35A and 36: Chart 25A shows that in these crises convulsions may occur:

the convulsions may sometimes occur with the rise, and sometimes with the fall of blood-pressure. Extremely abrupt rises only, or abrupt falls only, may occur: the former is shown in Chart 42, and Chart 12 shows an extremely sudden rise, followed by an equally abrupt fall, which ended in death from hæmatemesis. It is probable that some of these crises are due to suddenly developing and brief vaso-motor relaxations or contractions, leading to variation in the volume of blood in the arterial system. Sudden falls should also lead to the suspicion of some bleeding, as in gastric ulcer.

Venesection is capable of bringing about a very considerable fall of blood-pressure, which in the course of a few hours may be restored; see Chart 26B.

Charts 30, 34, 40, 45 and 50 afford comparatively small opportunity for studying the hyperpiesis of the patients concerned; for example, in Chart 30 it was only observed for about four days, and even then showed that the pressure was a falling one. Chart 34 shows hyperpiesis only for six days; Chart 40 for five days; Chart 45 for seven days (and during a part of this time the blood-pressure was subnormal); Chart 50 shows hyperpiesis for only three days. It must be pointed out, however, that the hyperpiesis in these cases is very real, persisting for many hours on end, and, moreover, the threshold at which hyperpiesis is considered to begin has been set high—150 mm., so that the charts are not so insignificant as may appear to be the case at a casual glance.

Charts 18, 21, 23 and 27 call for special consideration. Charts 18 and 21 represent what may be spoken of as "apoplectic hyperpiesis," as both patients succumbed to cerebral hæmorrhage, the hearts weighing respectively at the post-mortem examination 11 oz. and $9\frac{1}{8}$ oz., slight hypertrophy being found in Case 21, but only marked brown atrophy in Case 18. From these points it is clear that the hyperpiesis as represented by the charts was probably of but short duration, and due to the increase of intracranial pressure caused by the cerebral hæmorrhage, rather than being a part effect of causes which led to cardiac hypertrophy.

Chart 23 shows a very modest degree of hyperpiesis, and would not have been included in the present series had it not been that the patient before admission had been under observation as an out-patient for hyperpiesis (244 mm.) and associated symptoms, suggesting that the chart expressed merely the terminal stages of a very real state of hyperpiesis: as the post-mortem examination showed, the surmise was correct, for the heart was very much hypertrophied and the conversion of marked hyperpiesis to that indicated in the chart was clearly demonstrated to be due to extensive infarction of the heart wall, which no doubt was responsible for the falling-off in power of this organ during the few days in which the blood-pressure chart was made. Chart 27 shows constant hyperpiesis during only forty-eight hours: at the post-mortem examination the heart was found to weigh only 8 oz., and showed no characteristic hypertrophy. Charts 18, 21 and 27 nevertheless indicate how very desirable it is, before a diagnosis of Hyperpiesia is made, to make observations for a number of days under conditions of rest. It is probable that if the blood-pressure is found to be raised above the 150 mm. level, the observations being made night and morning for four days con-

secutively, such a case will prove to be one of Hyperpiesia or cerebral hæmorrhage or both.

CARDIAC FINDINGS

I. Several problems arise as to the condition of the heart in cases of Hyperpiesia, and one obviously important one is the question which has often been raised, namely, can Hyperpiesia be detected clinically without the help of the sphygmomanometer by ordinary routine examination of the heart ?

1. Is left-sided cardiac hypertrophy revealed at post-mortem examination in all cases of Hyperpiesia ? So far as this series is concerned, left-sided cardiac hypertrophy was found in every case except the following ones : Cases 10, 18, 21, 22, 27 and 48.

With regard to Case 10, there can be no doubt that the chart proved the existence of hyperpiesis. The post-mortem report records the facts that the heart weighed 20 oz., and that the left ventricle was dilated : further, that although there was some atheroma of the aortic valves and of the aorta, no valvular incompetence is recorded. The clinical examination gave complete support to the diagnosis of left-sided cardiac hypertrophy. It may therefore be safely presumed that this case was one in which the pathologist had inadvertently omitted reference to left ventricular hypertrophy.

Case 18 has already been referred to as an unsatisfactorily determined example of Hyperpiesia. The probabilities are that such hyperpiesis as was observed was of an "apoplectic" origin only. No mention whatever is made in the post-mortem report of cardiac hypertrophy affecting the left ventricle : indeed there was no great increase in the weight of the heart (11 oz.), and this could be readily explained by the presence of mitral valvular disease. The clinical support for the existence of left ventricular hypertrophy was misleading, as no murmur could be heard to indicate the mitral disease found at the post-mortem examination, and the clinical signs of heart disease noted could be accepted as just as good evidence of dilatation as of hypertrophy. This case has been excluded from the series as not being an example of Hyperpiesia. Observations on the blood-pressure have been made in so many cases of simple mitral disease without finding hyperpiesis, that the conclusion has been drawn that when hyperpiesis does occur in mitral valvular disease, it is independent of the latter, *e.g.* Case 24 of this series.

Case 21, in which the heart only weighed $9\frac{1}{2}$ oz. and was not hypertrophied, has also been excluded from this study, and the chart has been considered one of mere "apoplectic hyperpiesis."

Case 22 revealed at the post-mortem examination a heart-weight of $12\frac{1}{2}$ oz., but a left ventricular wall of "normal" thickness. Clinically the aortic second sound was once noted to be a little accentuated. On reference to the character of the charts of this case it will be seen that there was very definite hyperpiesis on many occasions. It must therefore be concluded, as in Case 10, that some error of observation has crept in, and that the condition of the wall of the left ventricle was wrongly reported.

CASE 27 is another example of absence of left ventricular hypertrophy, which is confirmed by the fact that the heart-weight was only 8 oz. There was only one piece of clinical evidence to support the view that the left ventricle was hypertrophied, namely, that the maximum impulse was in the nipple line. Evidently this was due to dilatation of the heart only, for the heart muscle was found post-mortem to be friable and soft. The blood-pressure chart, too, as already noted, showed that there was not continuous hyperpiesis for four consecutive days. The case was not one of Hyperpiesia, and is excluded from the study.

CASE 48 appears to be like Cases 10 and 22. The chart certainly indicates that the case was one of Hyperpiesia. The clinical examination gave some support to the view that the left ventricle was hypertrophied, though it was slender. The post-mortem report states that the heart weighed 15 oz.: no other abnormality was reported. Clinically this case is clearly one of Hyperpiesia, and left-sided ventricular hypertrophy may be assumed.

It will thus be seen, after removal from the list of the fifty cases of the three cases (Nos. 18, 21 and 27) which were not fully established clinically as cases of Hyperpiesia, that hypertrophy of the left ventricle was present in all the remaining cases. Hypertrophy of the left ventricle of the heart is a constant feature of cases in whom the blood-pressure has been found to be raised for four or more consecutive days.

2. How often was characteristic hypertrophy of the left ventricle able to be detected by clinical examination without the corroborative use of the sphygmomanometer to establish Hyperpiesia?

In ordinary clinical examination the left ventricle was considered to be probably hypertrophied if the maximum impulse was more forcible than usual, and (or) outwardly dislocated without the discovery of any cause for dilatation. If the aortic second sound was accentuated the existence of hypertrophy of the left ventricle was still more likely.

(*a*) Forcible and (or) outwardly dislocated maximum impulse. This was found in Cases 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, 17, 20, 23, 24, 25, 26, 28, 29, 30, 31, 33, 34, 35, 36, 37, 38, 42, 44, 45, 46, 47, 48, 49, 50—that is to say, in thirty-seven of the forty-seven cases in whom characteristic hypertrophy of the left ventricle was found post-mortem, *i.e.* 78 per cent.

(*b*) No mention of the character of the impulse was made in Case 43.

(*c*) Forcible and (or) outwardly dislocated maximum impulse was not found in Cases 11, 15, 16, 19, 22, 32, 39, 40, 41—that is, in nine of the forty-seven cases.

It is, of course, possible that other factors were present which could account for the forcibility and dislocation of the maximum impulse, *e.g.* aortic and mitral regurgitation. Reference has already been made to the fact that mere mitral disease is, in an extremely large proportion of the cases, accompanied by a normal or subnormal blood-pressure, so that when hyperpiesis has been found to exist in cases with evidence of mitral disease, proved to be due to endocarditis by post-mortem examination, it is legitimate to infer that such cases were examples of the existence of two independent conditions, Hyperpiesia and mitral endocarditis.

With regard to the behaviour of the blood-pressure in aortic valvular disease, observation on many cases has shown that it, too, may be normal or subnormal; but some cases reveal very "remittent" or "intermittent" features, that is to say, in the same day the systolic pressure may be raised above the normal at one time and be subnormal at another. In a series of cases of uncomplicated aortic valvular disease, due to endocarditis, no case yielded a characteristically hyperpiesic chart—that is to say, one in which the blood-pressure was constantly raised throughout for four or more days. Again, it seems legitimate to infer that cases showing aortic valvular endocarditis and Hyperpiesia are examples of the occurrence of two distinct diseases in the same patient.

Of the forty-seven cases those who were found by post-mortem examination to show aortic and (or) mitral valvular endocarditis are Nos. 2 (mitral); 16 (mitral); 22 (aortic); 24 (mitral); 26 (mitral); 29 (aortic and mitral); 35 (aortic and mitral); 36 (aortic); 37 (mitral); 41 (aortic and mitral); 43 (mitral); and 45 (mitral), *i.e.* twelve cases. Some of these cases revealed murmurs, the characters of which led to the suspicion of the particular valvular endocarditis, namely, Cases 2, 22, 24, 29, 35, 36, 37, 41 and 45. Cases 16, 26 and 43 revealed no murmurs at the bedside, though valvular disease was found post-mortem.

It is further possible that the forcibility and dislocation of the maximum impulse might have been due to right-sided pleural effusion or to left-sided pulmonary fibrosis and contraction. The latter condition was not found in any of the cases. Right-sided pleural effusion was met with in Case 15 (empyema) and in Cases 40 and 41 (serous effusion), but in these three cases the maximum impulse was not altered in force or position. Right-sided pleural effusion occurred in cases showing dislocation of the impulse to the left in only two cases, namely, Cases 45 and 47.

It is thus seen that the increased forcibility and (or) outward dislocation of the maximum impulse of fourteen of the above thirty-seven cases showing these abnormalities could have owed such manifestations to causes other than hypertrophy of the left ventricle from hyperpiesis; but at the same time it must be conceded that such abnormality in each of these fourteen cases might be due in part to hyperpiesis, because in the remaining twenty-three cases it was due to hyperpiesis and nothing else. The series of forty-seven cases therefore includes twenty-three cases for the study of left-sided cardiac hypertrophy, due to hyperpiesis only: these twenty-three cases (*i.e.* 48 per cent.) could all have been suspected to be cases of hyperpiesis without the help of the sphygmomanometer. In the remaining twenty-four cases (52 per cent.) left-sided hypertrophy of the heart would on ordinary clinical examination, without the use of the sphygmomanometer, have been attributed either to the presence of valvular disease or to the misleading effects brought about by a right-sided pleural effusion, or have been overlooked entirely. It was the sphygmomanometer alone which showed that in each of the twenty-three cases there was a something else which was in part, or wholly, responsible for the existence of the hypertrophied left ventricle, and that that something was the condition of Hyperpiesia.

Cases 11, 15, 19, 32, 39, 40 and 41, who revealed no forcible and (or) dislocated

impulse of the heart, would not have led to the suspicion of the existence of left-sided cardiac hypertrophy but for the use of the sphygmomanometer. If Case 16 is added to these seven, then it will be seen that 17 per cent. of the cases of hypertrophied left ventricle in which the hypertrophy was entirely, or in part, due to hyperpiesis would have been, but for the use of the sphygmomanometer, completely overlooked.

(*b*) Further clinical evidence of the existence of hypertrophy of the left ventricle was obtainable by the existence of an accentuated aortic second sound. This sign was heard in Cases 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 13, 14, 15, 16, 20, 23, 24, 25, 26, 28, 29, 30, 32, 33, 35, 37, 38, 40, 41, 46, 47, 49 and 50, that is in thirty-three cases. This sign was absent in Cases 12, 17, 19, 34, 42 and 48, that is in six cases. No mention of its occurrence or not was made in Cases 1, 22, 31, 36, 39, 43, 44 and 45, that is in eight cases.

There are, however, other causes for accentuation of the aortic second sound than hypertrophy of the left ventricle, and more especially in the case of aneurysm of the aorta, in uncovering of the first part of the aorta by adjacent pulmonary contraction and by the consolidation of the adjacent lung in pneumonia, which leads to the better conduction of the aortic second sound. In no case was an aneurysm or right apical pneumonia found which could have operated in this way. Cases 11 and 26 had extensive tuberculous disease of the upper lobe of the right lung, which may have accounted in part for the accentuation of the aortic second sound. Thus in thirty-two out of the forty-seven cases (68 per cent.) accentuation of the aortic second sound was present and gave a direct clue to the existence of hypertrophy of the left ventricle, and this accentuation was due to no other cause than hyperpiesis. In thirteen of the remaining fifteen cases, about 28 per cent., with absence of accentuation of the aortic second sound, the sphygmomanometer gave the true diagnosis. In two cases, fibrosis, etc., of the right lung could have accounted for the accentuation in part.

II. Another important problem which has been raised by the study of this series of cases is connected with the weight of the heart in cases of Hyperpiesia. It would be expected that a heart showing left-sided hypertrophy would be increased in weight, but it is clear that increase in weight in such cases may be due not only to left ventricular hypertrophy : the walls of the remaining three chambers of the heart may hypertrophy especially, if, as a result of leakage of the mitral valve, congestion occurs in the pulmonary circuit. It is for this reason that left-sided ventricular hypertrophy is a better gauge of the direct effect of hyperpiesis upon the heart than the total weight of the organ. So striking, however, is the enlargement of the heart in the majority of the cases of this series that it is felt desirable to record the weights of the heart in each of the forty-seven cases. It is known that the average weight of the heart in a man is 11 oz., and in a woman 9 oz., in health. In only one of this series did the weight of the heart approximate closely to these figures. In Case 31, a woman, whose age was 37 years, the body-weight was 6 st. 8 lb., the heart weight 11 oz., and the wall of the left ventricle was thickened, presumably from hypertrophy. In this case it

looks as if the heart-weight was not far from normal, but it will be observed that the woman was less in weight than the average, because the height and age of

TABLE I.

This Table shows the cases of the series, arranged according to the ages, in whom there was hyperpiesis and hyperpiesic hypertrophy of the left ventricle, uncomplicated by the presence of valvular endocarditis. The greatest increase of cardiac weight is not found at the greatest ages in either sex. The weights of the heart and kidneys are also shown.

No. of Case.	Age.	Heart Weight in ozs.	Total Kidney Weight in ozs.
MEN (29).			
6	27	16	8
15	29	19	5
35	29	24	13
38	36	13½	4
33	38	21	7
5	39	15	18½
3	41	17	9
42	41	25	19
20	42	23	9
39	42	21½	5
46	42	39	20
19	43	20	6
8	45	22	6
28	46	18	6
50	50	13½	8
10	52	20	7
49	52	21½	8½
13	54	13	12
34	55	15	14
47	56	20	7
11	59	17	7½
30	60	18	8
32	62	19	12
40	67	22	11½
9	68	18	7½
12	69	18	10
23	69	18	12½
48	70	15	13½
44	76	19½	14
WOMEN (6).			
1	26	13	5
14	33	17¼	12½
31	37	11	6
4	40	16	6
17	40	14	11
7	43	14	5

women of stature of only 4 feet 10 inches is 8 st. 8 lb., and so far as can be remembered this woman was about 5 feet 2 inches, the average weight for which at her age is 8 st. 12 lb., and when it is also noted that the left ventricle showed

thickening of the muscular wall, or hypertrophy, it may be assumed with safety that the heart in this case was increased in weight. It has been quite impossible to make the ideal comparison of heart-weight and total weight of voluntary muscles, and it is fallacious to make a comparison between the heart-weights of the patients of this series and the total weight of their bodies, seeing that some were fat, some were thin, some were œdematous, whilst some were free from œdema. It will be remembered that in the series of cases under examination thirty-six were males: excluding from this number those who had valvular endocarditis, which in itself could produce hypertrophy of the walls of the heart (Nos. 16, 22, 29, 36, 41, 43 and 45) and consequent increase of the weight of the heart, there were left twenty-nine cases in whom the hypertrophied left ventricle was of a purely hyperpiesic origin. The average weight of the whole heart in these twenty-nine cases was 18 oz. Similarly, excluding the cases of valvular disease (Nos. 2, 24, 26, 35 and 37) from the list of eleven women belonging to the series, the average weight of the hyperpiesic hearts amongst them was only a little over 14 oz. The weights of the hearts in the twenty-nine males varied from a minimum of 13 oz. to a maximum of 39 oz., and amongst the six women the minimum was 11 oz. and the maximum $17\frac{1}{4}$ oz.

Table I. shows the heart-weights of the purely hyperpiesic cases of this series, and it will be noted that the weight of the heart in Case 46 was 39 oz., the age being 42 years, and the body-weight 11 st. 12 lb., whereas in Case 44 the heart-weight was $19\frac{1}{2}$ oz., the age being 76 years, and the body-weight 9 st. 7 lb. The younger subject had the much heavier heart (being twice the weight) than the older subject. The appeal, therefore, to the weight of the heart does not support the view that the blood-pressure at any adult age may be measured by adding the number of the years of age to 100. It is, moreover, well known that extreme old age may be free from hyperpiesis and hypertrophy of the heart, whilst both abnormalities may be met with in children.

III. In Table I. the weights of the heart and of the kidneys are set out in those cases of this series which showed hyperpiesic left-sided hypertrophy of the heart, independent of any valvular disease. The weights of the kidneys will be seen to vary in the extreme from a total kidney-weight of 4 oz. as a minimum to a total kidney-weight of 20 oz. as a maximum. Supposing the average weight of a kidney in a healthy adult is 4 oz., then only three cases of the series presented kidney-weight of the normal amount of 8 oz., namely, 6, 30 and 50. The weight was less than normal in fifteen cases, namely, Nos. 1, 4, 7, 8, 9, 10, 11, 15, 19, 28, 31, 33, 38, 39 and 47, and was greater than normal in seventeen cases, namely, Nos. 3, 5, 12, 13, 14, 17, 20, 23, 32, 34, 35, 40, 42, 44, 46, 48 and 49. It is quite obvious that the weight of kidney substance does not run parallel with the weight of the heart. Further, as Mr. Lawrence's pathological observations show, a small atrophied kidney was found to be of greater weight than a kidney of normal size and structure (Case 36). Another point of great importance and interest to which reference may be made at this stage is, that the largest kidney met with in the series, giving a total kidney-weight of 20 oz., in Case 46, that is

150 per cent. increase in weight, showed trifling histological change. In other words, it looks as if the kidney could undergo hypertrophy, which, as Mr. Lawrence points out, is independent of any process of compensation, and for which no cause has yet been discovered: the heart weight of the patient was 39 oz.

IV. *Hyperpiesic murmurs.*—Leakage at valvular orifices of the heart from mere dilatation, *i.e.* without deformity of the valves from endocarditis, independent of dilatation of the valvular rings from weakening of the cardiac tissues, etc., and dependent merely upon the forcible distension of the valvular ring in hyperpiesic hypertrophy has been said to occur. Such effects would produce murmurs, which for distinction's sake may be called "hyperpiesic" murmurs. A diastolic murmur of this nature was heard at the aortic cartilage in Case 32, and the post-mortem examination showed that the aortic valves were incompetent. It is remarkable that this was the only case in which a hyperpiesic diastolic murmur was heard. Systolic murmurs of hyperpiesic origin were heard at the maximum impulse of the heart in Cases 3, 8, 23, 38, 44 and 46, from dilatation of the mitral ring, which was confirmed by post-mortem examination, so far as Cases 3, 8, 23 and 46 were concerned. Cases 38 and 44 revealed no definite enlargement of the mitral ring post-mortem. Cases 20 and 42 showed dilatation of the mitral ring post-mortem, and yet during life no murmurs had been heard over the maximum impulse. Thus the sphygmomanometer may be made use of to distinguish murmurs of hyperpiesic origin from murmurs which occur in valvular deformities due to endocarditis, because hyperpiesis, as already pointed out, is known not to occur in valvular deformity produced by endocarditis.

V. *Tortuosity of the brachial artery.*—In estimating changes in the arteries it will be seen in the reports of the cases of this series that reference has been made only to tortuosity, and the most accessible artery for this purpose was considered to be the brachial artery, and especially that part of it above the elbow-joint. Reference to the tortuosity of the temporal artery was open to the fallacy that that artery may be tortuous independent of pathological change. It is usual in cases in whom the brachial artery is normal to find that bending of the elbow is not followed by any marked demonstration of tortuosity, whereas it was very common in hyperpiesis to find that under these conditions the brachial artery showed marked tortuosity; in some cases the tortuosity of the brachial was obvious without bending the elbow. In both these latter conditions it may be assumed that whatever is responsible for hyperpiesis has led to the loss of power of the artery to regain its original axial length, either as the result of deterioration of the elastic elements of the arterial wall, or from an associated rise of diastolic pressure which, combined with the systolic high blood-pressure, permanently increased the axial length of the artery.

In this series of forty-seven cases tortuosity of the brachial artery was observed on forty occasions. Apparently the condition of the brachial artery was not studied in three cases. It has been found that the presence of abundant subcutaneous fat made this observation difficult or impossible. Tortuosity of the brachial artery could not be established in four cases, for example, Nos. 1, 34, 35

and 42. Case 1 was a young woman, æt. 26 years, in whom the hyperpiesis was moderate and the heart weight only 13 oz. Case 34 was a well-nourished man, æt. 54: he too showed moderate hyperpiesis; it is probable that his well-nourished condition made the tortuosity less visible. Invisibility of the brachial artery owing to the high degree of nourishment of the body was also probable in Cases 35 and 42. Another explanation is possible, especially in the younger subjects, as Case 1, namely, that the cause or causes producing hyperpiesis had not operated for sufficiently long time to produce the deformity. Tortuosity of the brachial artery was present in a large proportion of the cases in this series who were over 40 years of age. When tortuosity of the brachial artery occurs in cases of hyperpiesis the former does not precede, but succeeds the latter.

It is well known that tortuosity of the brachial artery may be found in those who are not the subjects of hyperpiesis. One explanation may be that such cases have had hyperpiesis, but that it has passed off; for example, if Case 20 had come under observation for the first time in April to June 1909, he would have been found to have tortuous brachial arteries, and the blood-pressure chart taken for three months continuously would have shown no hyperpiesis, and yet examination of Charts 20A and 20B, which had been taken before April 1909, show that hyperpiesis had been present in January 1909 and in March 1909. In other words, it is clear that tortuous brachial artery may be evidence of past hyperpiesis. Another way to explain the tortuous brachial artery occurring in the absence of hyperpiesis is that the arteries have become lengthened, not as a part result of the cause or causes of Hyperpiesia, but as a result of that intermittent increased systolic blood-pressure which occurs in those who perform heavy manual work. Tortuosity of the brachial artery is therefore a much less reliable sign of the existence of hyperpiesis than is left-sided cardiac hypertrophy in the absence of valvular disease, or accentuation of the aortic second sound in the absence of adjacent lung disease, aneurysm, etc.

DROPSY

Dropsy was found in a considerable number of the forty-seven cases of hyperpiesis. It varied from a slight manifestation in the feet to well-marked œdema of the feet and legs, even accompanied by ascites, dropsy of the body and hydrothorax and hydropericardium. It happened that the dropsy which was present occurred in some of the cases which were found to have also evidence of chronic valvular disease, so that these cases may not be looked upon exclusively as cases of hyperpiesic dropsy. At first sight it seems improbable that when the heart is working so vigorously, as it does in cases of hyperpiesis, dropsy should occur at all: moreover, it will be seen from the accompanying table that fever occurred in such a large proportion of the cases and was dependent upon obvious infective processes which were shown at the post-mortem examination, such as pericarditis, pleurisy, empyema, cellulitis, meningitis, tuberculosis, etc. There is therefore room for the view that the dropsy found in the cases of hyperpiesis is merely an expression of infection; but, as will be seen from Table II., there was one case (Case 12) in

whom dropsy occurred, but who showed no fever, and at the post-mortem there were no signs of inflammation anywhere. This case seems to point to the possibility that uncomplicated hyperpiesis may show dropsy. In view, however, of the great frequency of the occurrence of fever at some time or other in these cases of hyperpiesis, and in view of the fact that so often some infective focus was found post-mortem in those who had dropsy, it is reasonable to think that probably all cases of dropsy occurring in hyperpiesis are due to the toxic effects resulting from an infection which may, or may not, produce local inflammatory lesions. This question cannot be so easily settled, because it is not usual for cases of pleurisy, pericarditis, empyema, meningitis and cellulitis, occurring as primary disorders, to cause dropsy and ascites. As the accompanying table (Table II.)

TABLE II.—THE OCCURRENCE OF DROPSY, FEVER AND INFLAMMATORY SIGNS IN THIRTY-FIVE CASES OF HYPERPIESIA UNCOMPLICATED BY VALVULAR DISEASE OF THE HEART

No. of Case.	Dropsy.	Fever.	Evidence at Post-mortem of Infection.
1	o	+	Nil
3	+	+	Pericarditis
4	o	o	Pericarditis, pleurisy, broncho-pneumonia, petechiæ
5	+ (and ascites)	+	Erysipelas
6	o	+	Nil, but petechiæ
7	o	+	Pericarditis, broncho-pneumonia, purpura
8	+	o	Pericarditis, purpura
9	o	+	Empyema, pericarditis
10	o	o	Pneumonia
11	o	+	Bronchitis
12	+	o	Nil
13	+	+	Empyema
14	o	+	Pericarditis, recent endocarditis, bronchitis
15	+	+	Pericarditis, pneumonia, empyema
17	+	+	Nil, but purpura
19	o	o	Broncho-pneumonia, petechiæ
20	+ (and ascites)	+	Empyema
23	o	+	Pericarditis
25	+	+ (rigors)	Mucous colitis, pericarditis, pleurisy, broncho-pneumonia, petechiæ
28	+	+	Pericarditis, bronchitis
30	o	+	Nil
31	+ (and ascites)	+	Cellulitis of face
32	+	+	Meningitis
33	+	+	Pericarditis, pleurisy, pneumonia, petechiæ
34	o	+	Broncho-pneumonia
38	o	+	Nil
39	+ (and ascites)	+	Pericarditis, pleurisy and purpura
40	+	+	Pleurisy and pneumonia
42	+ (and ascites)	+	Pleurisy
44	+	+	Old adherent pericardium, petechiæ
46	+ (and ascites)	+	Nil
47	+	+	Pericarditis and pleurisy
48	o	o	Nil
49	+	+	Pleurisy, cellulitis of face
50	o	+	Nil

shows, moreover, these complicating inflammations occurred in some cases in whom dropsy was absent. Another point of interest is that pericarditis, etc.,

occurred so often without any temperature, a fact well known of course in pathology, but of particular interest in this study because inflammatory complications occurred so readily without affecting the temperature. On more than one occasion the discovery of the development of dropsy and of petechiæ (or purpura) has led to a more particular examination with the view of discovering one or other of the above inflammatory complications, and with positive results. Of the thirty-five cases of hyperpiesis, uncomplicated by valvular disease, dropsy was present in twenty cases and was absent in fifteen cases. Fever of long or short duration was found in twenty-nine cases, and was absent in six cases. Some complicating inflammatory process such as pericarditis, pleurisy, etc., was present in twenty-six cases and absent in nine. Purpuric manifestations were found in nine cases, and in only two of these was there absence of localised inflammation like pericarditis, etc.

Dropsy and effusions into various serous cavities are well-known manifestations of various renal disorders; and as the condition of the kidneys in this series varied from normal to extremely abnormal conditions the possible connection of the dropsy, etc., with renal disease must be considered (see later).

ALBUMINURIA AND CASTS

Albuminuria was tested for in the great majority of the forty-seven cases of hyperpiesis by means of heat and acetic acid. No doubt the use of this test has led to the detection of cases in whom nucleo-protein alone was present, as well as to cases in whom the proteins of the plasma of the blood were escaping into the urine. To reduce this possible error, casts were looked for in a considerable number of cases, for it was felt that this additional information would, in cases of albuminuria, give clearer indication of renal disease. It has long been considered that the occurrence of hyaline and granular casts in the urine is not necessarily an indication of disease in the kidney, whereas fatty and epithelial casts afforded more certain evidence of disease in this organ. The association of albuminuria, albuminuric retinitis, dropsy and renal disease, as shown in this series, will be studied at a later stage. In the following grouping, when reference is made to casts, it includes any form of casts, and, as above indicated, albuminuria means the protein reaction given by heat and acetic acid.

I. (*a*) Albuminuria was found to be present on *every* occasion on which the urine was examined for albumen, and was also found to be associated with the presence of casts on one or more occasions in the following cases: Nos. 1, 7, 14, 25, 32, 35, 38, 40, 46, 47—that is, in ten cases.

(*b*) Albuminuria was present on *every* occasion on which the urine was tested for albumen, but with negative findings as regards casts in the following cases: Nos. 4, 9, 15, 33, 39, 42, 48, 49, 50—that is, in nine cases.

(*c*) A number of cases when examined for albumen were *always* found to show this abnormality, but casts had not been looked for: these cases were Nos. 3, 5, 6, 10, 17, 19 and 43.

II. (*a*) Albuminuria was found on *some* of the occasions upon which it was looked for, and casts had been found at one time or another : the cases were Nos. 8, 11, 16, 20, 22, 26, 31 and 44—that is, eight cases.

(*b*) *Occasional* albuminuria and absence of casts were noted in two cases, Nos. 28 and 34.

(*c*) *Occasional* albuminuria was found in a certain number of cases, but casts were not looked for : these cases were Nos. 2, 12, 23, 24, 29, 30, 36, 41, 45.

III. Albumen was absent when looked for, and casts were found in Case 37. Albumen was absent when looked for, and no observations were made for casts in Case 13.

RETINAL CHANGES

Under this heading were included the following appearances : retinal hæmorrhages, patches of exudation in the neighbourhood of the macula, or in the neighbourhood of the optic disc and papill-œdema. The association of this phenomenon in the above grouping of albuminuria and casts is as follows :

Group I.	(*a*).—Retinal change	was	present in	Cases 7, 14, 25, 32, 35, 38 (6).
	,,	,,	,,	absent in Cases 1 and 46 (2).
	,,	,,	,,	not looked for in Cases 40 and 47.
	(*b*) ,,	,,	,,	present in Cases 4, 15, 33, 39, 42 (5).
	,,	,,	,,	absent in Cases 48, 49 and 50 (3).
	,,	,,	,,	not looked for in Case 9.
	(*c*) ,,	,,	,,	present in Cases 3, 6, 17 (3).
	,,	,,	,,	absent in Case 19 (1).
	,,	,,	,,	not looked for in Cases 5, 10 and 43.
Group II.	(*a*) ,,	,,	,,	present in Cases 8, 22 and 31 (3).
	,,	,,	,,	absent in Cases 11 and 20 (2).
	,,	,,	,,	not looked for in Cases 16, 26 and 44.
	(*b*) ,,	,,	,,	present in Case 34 (1).
	,,	,,	,,	not looked for in Case 28 (1).
	(*c*) ,,	,,	,,	present in Case 2 (1).
	,,	,,	,,	absent in Cases 12, 24, 36 and 41 (4).
	,,	,,	,,	not looked for in Cases 23, 29, 30 and 45.

Group III.—Retinal change, associated with absence of albumen and the presence of casts occurred in Case 37. No retinal change was noted in Case 13.

The changes in the retinæ of a hæmorrhagic character may be expressive of the occurrence of bacterial infection, which in the case of the skin and mucous membrane shows itself as petechiæ, purpura, submucous hæmorrhages, epistaxis, conjunctival hæmorrhages, hæmatemesis, melæna, hæmaturia, etc. Retinal change consisting of the characteristic white patches round the macula or irregular patches round the disc or swelling of the disc, or slighter changes than these, such as haziness of the retina and disc, are seen to occur with constant albuminuria or occasional albuminuria. The association with albuminuria is, as is well known, very variable, for though albuminuria is often found, yet any particular specimen of urine may fail to show it, though casts may be present in such a case.

It has long been known that albuminuric retinitis, though not indicative of any special form of kidney disease, is very prone to occur in these forms of chronic

interstitial nephritis which have led to granular kidney, widespread disease being found in the renal and retinal arteries : other observers consider that similar but distinctly different changes may occur in the retinæ without any kidney disease, but simply referable to disease of the arteries of the retinæ.

The impression has gained ground in some directions that albuminuric neuro-retinitis is certain proof that the kidneys are gravely altered by disease, and that the occurrence of this abnormality may complete the diagnosis of granular kidney in cases who without its presence could not be so diagnosed.

Special attention is invited to four cases, Nos. 2, 14, 17 and 42. In all four cases albuminuric retinitis was found. There was no other cause found at the post-mortem examination, such as intracranial tumour, which could have provoked kindred signs. In Case 2 it will be seen that the pathologist described the case as being one of death from chronic Bright's disease and mitral regurgitation. Microscopically 90 per cent. of the Malpighian corpuscles were capable of functioning. Capsulitis was responsible for the destruction of 10 per cent. of the Malpighian corpuscles and for the slight glomerulo-tubular atrophy : there was only slight arterio-sclerosis. The kidneys weighed 7 and $7\frac{1}{2}$ oz. respectively ; they were large, the capsules were adherent, and on removal left a slightly granular surface. The heart weighed 23 oz. It is quite clear that this was not a case of true granular kidney. Case 14 was described by the pathologist as one of fibroid kidneys, uræmia, bronchitis, endo- and pericarditis : there was marked arterial disease in the kidneys, especially in the interlobular arteries ; 70 per cent. of the Malpighian corpuscles looked capable of functioning : 30 per cent. of the corpuscles were destroyed : there was considerable tubular atrophy, in part due to arterial disease, and in part resulting from the capsulitis which destroyed the glomeruli. The heart weighed $17\frac{1}{4}$ oz., and the left ventricle was characteristically hypertrophied : the coronary arteries were almost occluded : the kidneys were somewhat enlarged and weighed $6\frac{1}{4}$ oz. each, the capsule was thickened, and when stripped off left a coarsely granular surface. Here, again, it cannot be claimed that the kidneys were typical examples of what is known as granular kidneys. Case 17 showed blurring of the optic disc and development of white patches in both retinæ. The post-mortem diagnosis was chronic nephritis, combined with acute nephritis, old pontine hæmorrhage, and recent pregnancy. The kidneys showed microscopically large areas of intense acute parenchymatous nephritis, as well as interstitial inflammation, due to infection ; 11 per cent. of the Malpighian corpuscles were destroyed and the remainder showed intense acute change : there was marked disease of both the arciform arteries and of the interlobular arteries : the kidneys were large, weighing $5\frac{1}{2}$ oz. each : the capsule was adherent, and on removal left a finely granular surface : the heart weighed 14 oz., and the left ventricle was hypertrophied and dilated. Case 42 showed marked albuminuric retinitis, with commencing "star-formation" in the right macular region. Special reference has already been made to this case because the pathologist at first reported that the kidneys appeared to be normal from naked-eye examination. When it was pointed out that during

life albuminuria had always been present, and that rather sudden death had occurred in a subject in whom electro-cardiograms had shown that the heart muscle was normal, in whom also marked albuminuric retinitis and retinal hæmorrhages had been observed, and that the pressure-chart was characteristic of Hyperpiesia; moreover, that the heart weighed 25 oz., and that hypertrophy was a feature, attention was again paid to the condition of the kidneys, which weighed 9½ oz. each, showed a slightly thickened, non-adherent capsule, very finely granular surface, with normal width of cortex and normal consistence on pressure. They were submitted to microscopic examination, with the result that the naked-eye description of the kidneys was largely confirmed : but the term chronic interstitial nephritis was substituted in deference to the clinical findings, and to the facts that 10 per cent. of the Malpighian corpuscles were found to be destroyed by former capsulitis, and that small scattered areas of tubular atrophy and fibrosis were met with in the cortex. It is clear, however, that these changes were such as might be met with in those whose kidneys would be considered normal had there been no clinical manifestations such as were met with in this case. There was only slight arterial disease.

These four cases cannot fail to interest the reader, because the sinister meaning of albuminuric neuro-retinitis has been admitted almost as an axiom, indeed it has been shown on an average that the duration of life may in the poor be limited to about fifteen months; in the well-to-do, five years.[1] These cases do not show that such a view is wrong, but they do point to the fact that albuminuric neuro-retinitis is not a certain indication, even when combined with other symptoms, all pointing to kidney disease, that such kidney disease will take the form of what is known as granular kidney. These four cases seem to point unmistakably to the assumption that even albuminuric neuro-retinitis, which of all the single signs indicating kidney disease is the strongest citadel of defence which has been raised by the advocates of the view that the state of the kidney is of such special importance in determination of clinical manifestations, is also a sign of a toxæmia resident in the blood ; but so far as this study goes its sinister meaning is not at all affected, though the reason implied by the qualification " albuminuric " neuro-retinitis long suspected to be based upon faulty pathology is clearly shown to be misleading, more particularly if the qualification albuminuric neuro-retinitis is considered to denote granular kidney (see also p. 130 *et seq.*), or any other form of grave kidney disease.

MODE OF DEATH

An attempt is made to classify the forms of death in accordance with contemporary, more or less clinical, conceptions ; for instance, some of the cases died of " cardiac failure " ; this included cases of death in which a valvular lesion was the chief abnormality: cases in whom the cardiac muscle was diseased, associated or not with occlusive disease of the coronary artery : in others, again, the only prominent abnormality was pericarditis.

[1] J. Herbert Parsons, *The Pathology of the Eye*, 1908, vol. iv. pp. 1297–8.

It is somewhat difficult to adopt a dogmatic position in regard to the mode of death of these cases. Where acute inflammatory changes have been met with in the heart, lungs, meninges or cellular tissues, such cases have been classified as cases of terminal infection; but it is at once clear that this group may include cases who clinically were thought to be suffering from, and even dying of, uræmia. Then, again, cases who appeared to die of uræmia were found to be associated with little or no change in the kidneys at all. In the list of forty-seven cases in whom the clinician in charge of the case made the diagnosis of "uræmia," such diagnosis has been accepted. In other cases the writer has himself, as the result of the perusal of the clinical records, and from personal clinical knowledge of the cases concerned, applied the term "uræmia." The modes of death may be roughly classified as follows:

I.	Uræmia (as stated by the physician in charge of the case), Nos. 5, 14, 22, 24, 35, 38, 49 (?)	7 cases.
II.	Uræmia (as diagnosed by the writer), Nos. 1, 4, 6, 7, 8, 15, 17, 39, 43 (?), 46 (?), 47 (?), 48	12 ,,
III.	Cases dying of terminal infection of various kinds, Nos. 9, 10, 16, 19, 20, 25, 26, 28, 31, 32 (?), 33	11 ,,
IV.	Cases dying of cardiac failure, Nos. 3 (?), 11, 23, 29, 36 (?), 40 (?), 41 (?), 42, 44, 45	10 ,,
V.	Cases dying from carcinoma of some part of the body, Nos. 12, 13, 30, 37	4 ,,
VI.	Cases dying of apoplexy, Nos. 34 (meningeal hæmorrhage), and 50	2 ,,
	Note that Cases Nos. 6 and 43 were also cases of apoplexy, but are included in Group 2 above.	
VII.	Death was sudden and completely unexpected in Case 2	1 ,,

ANALYSIS OF THE RECORDS OF THE CASES SAID TO BE URÆMIC (GROUPS 1 AND 2)

CASE 1.—Loss of consciousness and slight fits, albuminuria and casts. For three or four years vomiting, dyspnœa, and weakness.

P.M.—Granular kidneys, each weighing $2\frac{1}{2}$ oz. No terminal infection.

CASE 4.—Dyspnœa, headache, vomiting, giddiness, albuminuria, albuminuric retinitis, no casts, delirium, terminal fit.

P.M.—Red granular kidneys, weighing respectively $3\frac{1}{4}$ and $2\frac{1}{2}$ oz. Terminal infection—cardiac and pulmonary.

CASE 5.—"Hissing" breathing, restlessness, albuminuria.

P.M.—"Renal sclerosis," right kidney weighing 8 oz. and left $10\frac{1}{2}$ oz. Terminal infection—erysipelas.

CASE 6.—Attacks of loss of consciousness, twitching, drowsiness, dyspnœa, headaches, fits, albuminuria, albuminuric retinitis.

P.M.—Left cerebral hæmorrhage; red granular kidneys, each weighing 4 oz.: terminal infection—none reported, though petechiæ noted a year before death, and temperature had occurred with arthritis on several occasions.

CASE 7.—Headache persisting for years, morning sickness, albuminuria,

hæmorrhagic albuminuric neuro-retinitis, casts ; drowsiness, " sighing " breathing, twitching, petechiæ, occasionally slight fever : death in coma.

P.M.—Red granular kidneys, each weighing $2\frac{1}{2}$ oz. Terminal infections — pericardium and lungs.

Case 8. — Repeated fits during the last six days of life, Cheyne-Stokes breathing. Albuminuria thirty-seven times, negative on eight occasions, albuminuric retinitis, petechiæ after drainage : death in coma.

P.M.—Granular kidneys, each weighing 3 oz. Carcinoma of the rectum. Terminal infection—pericarditis. The death in this case was in no way due to the carcinoma of the rectum, which was moderate in size and caused no obstruction.

Case 14.—Headache for sixteen years periodically, accompanied by vomiting, the latter for four and a half months prior to admission, failure of sight three weeks prior to admission ; albuminuria and hæmaturia, hæmorrhagic neuro-retinitis ; casts present ; semi-comatose condition in hospital, purpura, occasional slight fever : death in coma.

P.M.—" Fibroid kidneys," each kidney weighing $6\frac{1}{4}$ oz. Terminal infection —pericarditis, endocarditis, bronchitis.

Case 15.—Vomiting for fifteen months prior to admission, which intensified and was accompanied by twitchings of the arms and retention of urine just prior to death. Albuminuria, albuminuric neuro-retinitis, no casts. Slight fever on one occasion.

P.M.—" Chronic Bright's disease," right kidney weighing 2 oz. and the left 3 oz., not granular but showing irregular areas of atrophy of the cortex. Terminal infections—pneumonia, empyema, and pericarditis. It is not easy to allocate the cause of death in this case. The attacks of sickness for fifteen months, which intensified and were accompanied by twitching just before death, are very suggestive that the patient was suffering from uræmia, but the post-mortem inflammatory findings and the pressure-chart suggest that the actual cause of death was terminal infection.

Case 17.—This patient was pregnant four months, and developed vomiting and headache, nose bleeding, hæmorrhage from the gums and profuse purpura. Miscarriage occurred, and the patient became semi-comatose. There was albuminuria and hæmaturia, albuminuric neuro-retinitis, twitching of the face : death in coma. Fever was present in slight degree.

P.M.—Chronic and acute nephritis, each kidney weighing $5\frac{1}{2}$ oz. No evidence of terminal infection except the acute nephritis.

Case 22.—Shortness of breath, morning sickness, drowsiness, fits, with loss of consciousness, twitchings, albuminuria, hæmaturia, albuminuric retinitis (also small hæmorrhage), hyaline and granular casts ; purpura, slight occasional fever, suppression of urine, coma.

P.M.—Red granular kidneys, each weighing 3 oz. Terminal infection—pneumonia.

Case 24.—For some considerable time whilst this patient was under obser-

vation her symptoms were those of cardiac failure, such as cough, palpitation, dropsy, shortness of breath, cyanosis, yellowness of the conjunctivæ, irregular pulse, enlargement of the liver (upwards) : albuminuria, present on fourteen occasions and absent on five, mitral murmur, with enlargement of the cardiac area. The dyspnœa was paroxysmal in type. Effusion occurred in the chest, and its removal gave little or no relief. Four days before death—so runs the clinical report—she had "a fit, probably of a uræmic nature." This fit was repeated several times before she died. The temperature was raised for a few days after admission only. The funduses of the eyes were normal.

P.M.—There was stenosis of the mitral valve : the right kidney weighing 6 oz. and the left 7 oz. The kidneys were found to be merely congested. No terminal infection.

The importance of this case cannot be exaggerated. She was under observation for a considerable period, and extended pressure-charts were able to be made : that one drawn up from April 9 to May 16 being a very well-marked one of hyperpiesis. The clinical diagnosis was, "A case of morbus cordis associated with granular kidney, as shown by mitral disease, pleural effusion, hypertension and uræmia." This verdict was a reasonable one, and yet at the post-mortem granular kidneys were not found, and the structural changes found in the kidneys microscopically were small ! Had it not been for the occurrence of the uræmic manifestations, the physician in charge of the case would almost certainly have attributed death to cardiac failure only.

Case 35.—The patient suffered from shortness of breath and feeling "out of sorts," and in 1910 developed violent headache, became unconscious, had a fit and bit his tongue. This convulsion was repeated soon after. A year later he was still short of breath and felt dazed and giddy. His breathing on admission was found to be laboured and periodic. There was albuminuria and hæmaturia, and he died in uræmic coma. There were hæmorrhages in both funduses : the temperature rose in the last twenty-four hours of life. Casts had been found in the urine. There was no cough.

P.M.—The kidneys showed chronic parenchymatous nephritis, weighing 7 oz. and 6 oz. respectively. Terminal infection—pneumonia at the base of the right lung.

Case 38.—Left-sided headache and morning sickness, nose-bleeding. Two years later the sight began to fail and hæmorrhagic albuminuric retinitis developed ; albuminuria, hæmaturia and the passing of casts occurred ; blindness became more marked and drowsiness set in : the breathing became "hissing" in character, and he died in a uræmic fit. Temperature was raised on occasions.

P.M.—Red granular kidneys, each organ weighing 2 oz. No terminal infection.

Case 39.—Shortness of breath, orthopnœa, dropsy, albuminuria, casts, hæmorrhagic albuminuric retinitis ; purpura, temperature occasionally raised, mania, vomiting, jerky movements : death in uræmia.

P.M.—Chronic interstitial nephritis in right kidney, which weighed 4 oz. ;

left kidney atrophied and weighing 1 oz: stone in the bladder. Terminal infection—pericarditis and pleurisy. Although during life the clinical aspect of the case partly suggested cardiac failure accompanied by symptoms of terminal infection as the cause of death, the physician in charge considered that uræmia was the real cause.

CASE 43.—Loss of consciousness. He had fits before admission, fifteen and four years previously, and also five weeks previously. Slight albuminuria, double extensor responses: temperature subnormal. The symptoms and signs before death suggested uræmia, but the actual cause of death was cerebral hæmorrhage.

P.M.—Cirrhosis of kidneys, each weighing $7\frac{1}{2}$ oz. Capsules not adherent. Right cerebral hæmorrhage. No terminal infections. Heart weight, $17\frac{1}{2}$ oz. Hypertrophy of the left ventricle.

CASE 46.—Dyspnœa, palpitation, "night starts," nycturia, orthopnœa, albuminuria, hæmaturia, casts; dropsy, cardiac murmurs, occasional temperature, positive Wassermann reaction. Finally, scanty urine, breathlessness and cyanosis; liver much enlarged; death quiet, but dyspnœa marked.

P.M.—Smooth large fibrotic kidneys, each weighing 10 oz. The heart showed hypertrophy and weighed 39 oz. No valvular lesion: no terminal infections.

This case showed comparatively slight pathological change in the kidneys, and the total weight of the kidney substance was greatly increased. The hypertrophy of the heart was extreme. The so-called uræmia observed in this case was of the cardio-respiratory form. Hyperpiesia as a fatal disease is exemplified by this case: it is impossible to find any cause for the fatal ending other than a toxæmia of an undefined nature.

CASE 47.—Dyspnœa, palpitation, Cheyne-Stokes breathing, insomnia, delirium; albuminuria, casts; occasional slight fever; death in coma.

P.M.—Chronic interstitial nephritis, each kidney weighing $3\frac{1}{2}$ oz. The cortex was reduced and irregular. Terminal infections—pericarditis and pleurisy; infarction of lung. It is questionable whether this case died of uræmia or of the terminal infections.

CASE 48.—Nausea, vomiting, insomnia, slight headache, albuminuria and hæmaturia, no casts (no changes in eyes), twitchings of arms and forearms, restlessness, alternating with drowsiness, no fever; finally death in coma.

P.M.—Malignant disease of the bladder, involving both ureteral orifices. Right kidney weighed $3\frac{1}{2}$ oz. (hydronephrosis), left kidney, 10 oz. (slight hydronephrosis). No terminal infections.

CASE 49.—Epigastric pain, vomiting, dyspnœa, palpitation, headaches, insomnia, nycturia, albuminuria (no casts), slight fever occasionally, slight twitchings and semi-comatose condition with death in coma. Cellulitis of the face, following extraction of teeth. Temperature did not rise to more than 99°.

P.M.—Red granular kidneys, right kidney weighing 4 oz. and left $4\frac{1}{2}$ oz. Terminal infections—pleurisy, cellulitis.

Symptoms of uræmia were clearly evident during life in this case, but it is doubtful whether he actually died of uræmia: it is possible that death resulted

from the terminal infection following teeth extraction on April 24, for the blood-pressure as shown by the chart fell from 220 mm. to 140 mm. at death ten days later.

Amongst this list of nineteen cases uræmia appears to be a feature, being responsible for the symptoms during life, and apparently in some cases in part for death. In other cases uræmia appears to be the one and only cause of death. Amongst these nineteen cases there will be seen to be seven classical cases of granular kidney, namely, Cases 1, 4, 6, 7, 8, 22, 38. In each of these cases the total weight of kidney substance was less than the average total of 8 oz. Case 15 was a case of atrophy of the kidney substance leading to diminution of the total weight to something less than 8 oz., but the atrophy was localised and did not produce the classical diffuse atrophy which constitutes a granular kidney. In Cases 39 and 47 the nomenclature of the kidney disease adopted by the pathologist was that of chronic interstitial nephritis : the presence of granulation of the surface had not been mentioned : the total weight of the kidneys was like that of granular kidney, less than normal.

It is, however, to be noticed that not in all the cases in whom uræmia was a symptom were the kidneys found to be granular or under weight ; for example, Case 5 was described as a case merely of renal sclerosis : the surfaces were only slightly granular and the total kidney weight was 18½ oz. In Case 14 the kidneys are described as fibroid, but the pathologist concerned stated that the capsule was thickened, and when stripped off, left a coarsely granular surface : the total kidney weight was 12½ oz. In Case 17 the kidneys were described, naked-eye, as being large, finely granular and being probable examples of the combination of acute and chronic nephritis : the total weight of the kidneys was 11 oz. Case 35 was described as a case of chronic parenchymatous nephritis with smooth surfaces, and the total kidney weight was 13 oz. Case 48 was an example of hydronephrosis of the right kidney, which weighed 3½ oz., with early hydronephrosis of the left kidney, which weighed 10 oz., making a total kidney substance of 13½ oz., which is above the normal. Case 49 was an example of red granular kidney, and the total weight of kidney substance was slightly over the average, namely, 8½ oz.

Uræmia, therefore, seems to be, as is accepted, not only a feature of granular kidneys of under-weight, but of granular kidneys of normal weight, and also of kidneys which are fibrosed without showing granularity, and of acute and chronic parenchymatous nephritis. From the above observations uræmia may be a feature occurring with slightly fibroid or almost normal kidneys ! In support of this last statement three cases may be considered more closely, namely, Cases 24, 43 and 46. In Case 24 it will be remembered that the uræmic manifestations were terminal only, and up to within a short period of death the case had presented the familiar features of cardiac failure, associated with valvular change ; but there was distinct evidence in favour of uræmia, namely, the development of convulsions : the blood-pressure charts showed marked hyperpiesis. It looks, therefore, as if uræmia, so far as its clinical manifestations are concerned, may occur in a person whose kidneys, as in this case, were so little abnormal that no special reference was

made to them in the abridged post-mortem diagnosis: even on microscopic examination the amount of change found in the kidneys was so small as to raise the question whether a perfectly healthy person dying from an accident might not show as little. Turning to Case 43 there was a distinct history of convulsive seizures fifteen years, five years and five weeks prior to admission to the hospital: in all other ways he appeared to have been a healthy man, until he had been admitted to the hospital comatose, from cerebral hæmorrhage. It may be felt that the evidence of existence of uræmia in this patient was exceedingly slender, and that the convulsive seizures above referred to may have been due to idiopathic epilepsy. The facts, however, that the heart was found to weigh 17½ oz., and that slight albuminuria had been present during life, and that the blood-pressure when taken reached as much as 256 mm., justify the view that this case was one of uræmic epilepsy. Accepting this view, the condition of the kidneys is remarkable; for as in Case 24 the microscopic changes in the kidney were very small. In Case 46 there was a much more suggestive history of kidney disease, and the physical signs supported this view. The clinician in charge of the case would probably have been in difficulties, because although there were cardiac signs which suggested valvular change, so many other features pointed to the case being one of kidney disease, and the dyspnœa which was such a feature was an example of the respiratory form of uræmia. At the post-mortem the heart was found to weigh 39 oz. and was otherwise normal; each kidney weighed 10 oz., and all that the pathologist could say of them was that they were examples of large fibrotic kidneys. The microscopic examination again shows the remarkable fact that as in Case 24 and Case 43 the microscopic departure of the kidneys from the normal was minimal and negligible. *In other words, uræmia may occur in individuals whose kidneys are normal in structure, but who during life showed hyperpiesis.* The nature of the toxæmia in these cases is unknown, but it is well known not to be uræmic *stricto sensu*. There is reason therefore for the assumption that in these cases there is some other toxæmia which operating produced the symptoms met with in these cases — a toxæmia which may be supposed to be the underlying cause of Hyperpiesia.

ANALYSIS OF THE RECORDS OF CASES WHO APPEARED TO DIE OF SOME TERMINAL INFECTION (Group 3)

Case 9 was a clear case of Hyperpiesia, with dislocation of the maximum impulse outwards and accentuation of the aortic second sound: albumen was constantly present in the urine. Post-mortem examination showed infarction of the lungs and a left-sided empyema: left kidney hydronephrotic and weighing 2½ oz., right kidney weighing 5 oz. and being of the "granular kidney" type. Total kidney weight, 7½ oz. Heart weight, 18 oz.

Case 10 was also an example of Hyperpiesia, accompanied by cardio-vasculo-renal changes. Dyspnœa became a marked feature during the last three weeks of life, and the patient died comatose.

P.M.—The heart weighed 20 oz., both kidneys were granular and scarred, and each weighed $3\frac{1}{2}$ oz., making a total weight of kidney substance of 7 oz. Double lobar pneumonia.

Case 16 gave a history of increased shortness of breath, dyspnœa and orthopnœa one month before admission: signs of bronchitis and pericarditis were audible; pleural effusion and general dropsy; albuminuria frequently found, also hyaline, fatty and granular casts; slight fever only on three separate days, and after about two months' stay in the hospital the pulse began to fail, dyspnœa increased and cyanosis occurred: the patient became unconscious a few hours before death.

P.M.—Hæmorrhagic pericarditis, red granular kidneys, weighing $5\frac{1}{2}$ and 6 oz., making a total kidney substance weight of $11\frac{1}{2}$ oz. Heart weight, 24 oz. There is no question that this patient died of uræmia, for the breathlessness was readily explained by the occurrence of pleural effusion and the effect upon the heart of the pericarditis. It is open to question whether this case succumbed from terminal infection or from cardiac failure. During the stay in the hospital, symptoms and signs of the latter were cardinal features, but the terminal inflammatory infections were so marked as to make it probable that the final complete cardiac failure was due to them.

Case 19 showed signs of pleurisy and broncho-pneumonia of the right lower lobe, and the clinical course, with the exception of the absence of fever, confirmed the diagnosis. Other than a little tortuosity of the brachial arteries and albuminuria there was little to suggest, apart from the chart, that the patient was also suffering from Hyperpiesia.

P.M.—The heart weighed 20 oz., the kidneys were red and granular and weighed 3 oz. each.

Case 20 was under observation for a considerable time, appearing to be one of characteristic Hyperpiesia, but signs such as dropsy and irregularity of the pulse were present, suggesting that the cause of the symptoms was cardiac disease, more particularly of the myocardium. The evidences of cardiac failure passed off after his first visit, but recurred and necessitated a return to the hospital. He became drowsy and very dyspnœic, the pulse became very feeble; he coughed up bloodstained expectoration and pericardial friction sounds were heard. Muscular twitching developed before death, and he died comatose.

P.M.—This revealed the presence of a left-sided empyema and infarction in both lungs; the heart weighed 23 oz., and the source of the infarction was probably myocardial disease, secondary to atheroma of the coronary artery: recent and old infarcts were found in the kidneys, and the non-scarred portion showed a granular surface. Each kidney weighed $4\frac{1}{2}$ oz., making a total kidney substance of 9 oz.

Despite the albuminuria and other signs suggestive of cardio-vasculo-renal changes, hyperpiesis and the muscular twitchings which he developed before death, the actual cause of death was probably due to the development of the empyema, because, as he showed in his first visit to the hospital, before an empyema

developed, he improved so much as to be allowed to go home. Here, again, it is debatable whether death should be attributed to the empyema or to myocardial degeneration from coronary artery disease, combined with infarction of various organs from ante-mortem clot found at the apex of the left ventricle. The extremely large empyema (5 pints) gives good reason for accepting the cause of death as being infection.

Case 25 showed evidence of cardio-vasculo-renal change; very definite fever was present on several occasions; even a rigor on one. Pericardial friction sounds were heard and mucous colitis became a prominent feature. It is possible that uræmia was present, seeing that the urine became scanty on one occasion; also vomiting, insomnia and great restlessness occurred; but petechiæ (showing the occurrence of infection) developed before death.

P.M.—This supported the view that death was brought about by the terminal infection of the pericardium, pleura and lung: the heart weighed 13 oz., and the kidneys were red and granular, the right one weighing 2 oz. and the left $2\frac{1}{2}$ oz., making a total kidney substance of $4\frac{1}{2}$ oz.

Case 26 was a case who was under observation for a considerable time. When first seen she was treated for "hypertrophy of the heart, arterio-sclerosis and granular kidney," and her cough and expectoration were considered to be symptomatic of this condition. The blood-pressure had been found to be very high on several occasions and albumen was found. Signs of tuberculosis of the right lung rapidly developed, and T.B. were found. The impulse of the heart, though still forcible, was no longer dislocated externally to the left nipple line, but approached closer to the sternum. The blood-pressure ultimately became subnormal, and the patient died as a case of advanced pulmonary tuberculosis.

P.M.—The heart weighed 14 oz., the left ventricle was slightly hypertrophied, the muscle substance was pale and friable: the right lung was extensively tuberculous, and the left less so. The kidneys were large and congested, the consistence was increased somewhat, and microscopically slight patchy "chronic interstitial nephritis" was found, with general cloudy swelling, probably due to toxæmia of chronic tuberculous infection. The right kidney weighed 9 oz. and the left one 8 oz.; total kidney substance, 17 oz. Clearly the cause of death was the pulmonary tuberculosis: the case is a singular one, showing how a case of Hyperpiesia may lose its characteristic feature under the influence of a chronic infection. Attention must be called to the extremely slight chronic change in the kidneys.

Case 28 came under observation for symptoms which were very suggestive, at first glance, of pulmonary tuberculosis. Hyperpiesis and cardio-vasculo-renal changes were discovered, as well as a left-sided pleural effusion. A little over a week before death pericarditis was discovered: the mental powers gradually failed and he died quietly.

P.M.—This showed no active pulmonary tuberculosis; the base of the right lung was congested and there was diffuse bronchitis. The heart weighed 18 oz., and each kidney 3 oz., making a total kidney substance weight of 6 oz., and they were red and granular in type.

Case 31 was admitted with suggestive uræmic symptoms, and there was evidence of cardiac hypertrophy, independent of valvular disease. About a fortnight before death herpes developed, and a very severe cellulitis supervened, which caused septicæmia and death.

P.M.—This showed the heart weighed 11 oz., and vegetations were found on the mitral valve. The kidneys showed a fine granular surface, weighed 3 oz. each, making a total kidney substance of 6 oz., and were described as examples of chronic interstitial nephritis.

Case 32, who had been under observation for a very considerable time, was first of all an obvious case of Hyperpiesia, even developing "uræmic" losses of consciousness. From all these symptoms he recovered sufficiently to be discharged. Three years later he was readmitted, having had a return of his "uræmic" convulsions. Retinal change found three years previously was again noted. When admitted he was conscious, but gradually symptoms and signs of meningitis developed, of which he died.

P.M.—The meningitis was found to be of a purulent nature, and dependent upon otitis media: death was due to an infection which would not be considered one of the usual terminal infections of Hyperpiesia. The heart weighed 19 oz., the left kidney was atrophied and weighed only 3 oz., the right kidney weighed 9 oz. and its surface was granular. The total kidney substance was 12 oz.

Case 33 was admitted with a history of epigastric pain and shortness of breath and the cardio-vasculo-renal changes of hyperpiesis were discovered: slight temperature was found fairly frequently and headache and difficult breathing: restlessness and delusions also developed, so that uræmia was feared. Pericardial and pleural friction sounds were detected, as well as petechiæ.

P.M.—Pneumonia, pericarditis and pleurisy were found; the heart weighed 20 oz., and each kidney weighed $3\frac{1}{2}$ oz., making a total kidney substance of 7 oz., and each was finely granular on the surface.

This group of eleven cases, who appeared to die of a terminal infection of an acute character, or of acute exacerbation of a chronic infection, affords an opportunity of studying the heart and kidneys in cases of Hyperpiesia, because but for the accident of the infection death would not have occurred till later. It gives an opportunity of seeing what may be called the hyperpiesic heart: that is to say, a heart in which hypertrophy may be present in the walls of each chamber, reaching its maximum in those of the left ventricle, the valves of the heart being free from any defect which would cause them to leak or to obstruct the flow of blood through the heart. This group of cases does not show the picture as clearly as some other cases of the series, because of the effects of pericarditis and of the other infections noted upon the cardiac muscle, possibly leading in some cases to a reduction in the degree of the hypertrophy of the muscle, and to actual softening due to degeneration in others. The weights of the hyperpiesic hearts varied considerably from a minimum of 13 oz. in Case 25 to a maximum of 20 oz. in Case 19; such weights providing but a rough estimate of the cardiac hypertrophy, because no doubt the weights in some hearts were increased by the addition of inflammatory products.

The condition of the kidneys in this group presented a variability, both in weight and general characters, similar to those of the cases who appeared to die of uræmia. Granular kidneys of total underweight were found in Cases 9 (7½ oz.), 10 (7 oz.), 19 (6 oz.), 25 (4½ oz.), 28 (6 oz.), and 33 (7 oz.). Case 31 showed a total kidney weight of only 6 oz., and the kidneys were described as examples of chronic interstitial nephritis, but as the capsule on removal left a finely granular surface, the case may be included as one of granular kidney. Four cases remain, showing a total kidney weight greater than normal—Case 16 was a case of red granular kidney, with a total weight of 11½ oz. ; Case 20 was a case of red granular kidney in which the granulations were described as being small, and yet the pathological nomenclature adopted for it was a red granular kidney ; recent and old infarcts were responsible for the irregularity of the remaining part of the cortex : the total weight of the kidneys in this case was 9 oz. Case 26 was one in whom the condition of hyperpiesis, with the usual cardio-vasculo-renal changes, was noticed when she attended as an out-patient for nearly seven years, before she was admitted to hospital when the charts shown were made. These charts do not provide much evidence of very protracted hyperpiesis, but for two years as an out-patient, before admission as an in-patient, she had on four occasions shown a blood-pressure of over 200 mm., and during the seven years prior to admission she had been found occasionally to be passing albumen. The weight of the heart (14 oz.) and the condition of the left ventricle show the organ to be of the hyperpiesic type : the total kidney weight was 15 oz., and only very patchy chronic interstitial nephritis was found : almost all the Malpighian corpuscles were normal : the tubular epithelium was swollen and undergoing partial granular disintegration. It may be presumed that this epithelial degeneration was merely an expression of the tuberculosis which gradually destroyed the patient, and that during the period of her undoubted hyperpiesis, when the tuberculosis was only in its initial stages, the kidneys were probably almost as near the normal as the three cases already referred to in the group of cases said to be uræmic in whom so little change was found in the kidneys, namely, Cases 24, 43 and 46. Case 32 is an example of atrophy of the left kidney from thrombosis of the artery supplying it with blood : the clot in this vessel was old-standing and organised : the remnant of the left kidney weighed 3 oz., making with the right kidney, which weighed 9 oz., a total kidney weight of 12 oz. : the right kidney showed a granular surface and cysts were seen in it : the left kidney showed a smooth surface. The speculation therefore may be made that with the destruction of the left kidney hypertrophy occurred in the right one, both organs originally presenting a smooth surface, and that later on the right one became granular. Terminal infection or chronic infection is thus shown also to be a potent cause of death in cases of Hyperpiesia.

ANALYSIS OF THE RECORDS OF THE CASES WHO APPEARED ON CLINICAL STUDY TO DIE OF "CARDIAC FAILURE" (GROUP 4)

CASE 3 had suffered from shortness of breath and dropsy, a feeling of giddiness, headache and vomiting : constant albuminuria. With appropriate treatment all

these symptoms disappeared, and, as Chart 3A shows, the hyperpiesis was lost: for two years he was free from symptoms, but at the end of that time was re-admitted for a recurrence of his symptoms; pericarditis developed, and the patient died in the third of a series of syncopal attacks. Despite the "cardiac" aspect of this case, no valvular lesion was ever detected, and albuminuric retinitis was discovered. It is quite clear that this case would have been considered by some observers to have died of uræmia (headache, vomiting, albuminuric retinitis and albuminuria); others, again, would have preferred to place the case in Group 3, as being one in whom a terminal infection had occurred; the recurrent syncopal attacks, however, give good excuse for speaking of the death, in the clinical sense, as one of "cardiac failure."

P.M.—The heart weighed 17 oz.; probable mitral regurgitation: recent pericarditis; red granular kidneys, each weighing $4\frac{1}{2}$ oz.

Case 11.—A stout, healthy-looking man who had suffered from repeated attacks of breathlessness. He was admitted for one of these attacks: no dropsy: albumen found on three occasions in ten examinations: funduses normal. Sudden breathlessness again occurred, waking him from sleep, and in ten minutes he was dead.

P.M.—This showed red granular kidneys ($3\frac{1}{2}$ and 4 oz.): heart showed hyperpiesic hypertrophy: weight, 17 oz.: fibroid degeneration of heart muscle: anterior coronary artery occluded by thrombosis.

Case 23 was a stout, florid-looking man who became giddy after making any muscular effort. Seeing that the cardiac sounds were very indistinct, that a systolic murmur was heard at the apex of the heart, that the urine was found free from albumen or blood, and that the blood-pressure whilst he was in the ward was not raised constantly, the view was taken (erroneously) that the cardiac muscle was being hampered by fatty infiltration. Death took place quite suddenly without any warning.

P.M.—This showed recent pericarditis, with adhesions of the pericardial layers, mitral leakage, thrombosis of a branch of the coronary artery, and infarction of the heart-wall. Heart weight, 18 oz.; red granular kidneys, weighing 6 and $6\frac{1}{2}$ oz. respectively. The absence of albuminuria was interesting.

Case 29 was admitted for shortness of breath, and gave a history of scarlet fever and of rheumatism: orthopnœa, cyanosis, irregular pulse, enlargement of the heart to right and left, systolic murmur at the apex, and systolic and diastolic murmurs at the aortic cartilage; albuminuria, which had been present, disappeared: death in an attack of severe dyspnœa.

P.M.—The heart weighed 24 oz.; aortitis, thickening and retraction of the aortic valves, thickening of mitral valve: red granular kidneys, each weighing 4 oz.

Case 36.—Dyspnœa for twelve months, insomnia, palpitation, cardialgia, dropsy, hæmoptysis, orthopnœa, cyanosis, enlargement of the heart to the right and left, systolic and diastolic murmurs at the aortic cartilage, intermittent albuminuria: death sudden, in an attack of faintness and dyspnœa.

P.M.—The heart weighed 26 oz., aortitis and dilatation of the aorta, dilatation of the aortic orifice; kidneys weighed $5\frac{1}{2}$ oz. each: surface finely granular, described as examples of chronic interstitial nephritis.

Case 40 complained of dyspnœa and palpitation on effort, insomnia, orthopnœa, constant albuminuria, right pleural effusion, œdema, Cheyne-Stokes breathing; the dyspnœa increased to sixty per minute at time of death: temperature rose the day before death.

P.M.—The heart weighed 22 oz., hyperpiesic in type: turbid right pleural effusion, lymph on the surface of, and infarct in the right lower lobe; pneumonia in the right middle and lower lobe, and the left lower lobe; the right kidney weighed $5\frac{1}{2}$ oz. and the left 6 oz., and each was described as "cirrhotic," the removal of the capsule tearing away kidney substance. This case was clinically considered to be a cardiac case, with probably enlargement of the liver and effusions at both bases; considerable surprise was caused by the post-mortem findings of inflammation which, however, were, strictly speaking, corroborative of the original view that the patient was suffering from cardiac failure, because, though pneumonia and pleural effusion occurred, these were probably dependent upon lung infarction, which originated from the faulty action of the heart.

Case 41 was a case of lymphocytic leucocythæmia with a history of rheumatic fever occurring at the age of 19: pains over the heart, dyspnœa, orthopnœa, insomnia; pleural effusions, ascites and dropsy, apical systolic murmur; rise of temperature just before death.

P.M.—The heart weighed 15 oz., narrowing of the aortic valve and of the mitral valve: the right kidney weighed $5\frac{1}{2}$ oz. and the left 6 oz., the surfaces were granular and the kidneys were described as examples of chronic interstitial nephritis. Death was attributable in this case rather to the valvular lesions than to the leucocythæmia, or to the septicæmia initiated by the incisions in the ankles, which caused cellulitis. There is reason, however, for attributing death to the cellulitis.

Case 42 suffered from pain in the front of the chest, dyspnœa, cough, insomnia, œdema of feet, orthopnœa, constant albuminuria, right pleural effusion, cyanosis, increasing feebleness of the pulse: sudden death.

P.M.—The heart weighed 25 oz., mitral and tricuspid orifices dilated; ante-mortem clot in left ventricle, adherent to wall, infarction of the lung and pleurisy; the kidneys weighed $9\frac{1}{2}$ oz. each, surfaces finely granular, described as examples of chronic interstitial nephritis. Death was due to the myocardial disease which presumably gave rise to the ante-mortem clot in the left ventricle.

Case 44 was admitted for shortness of breath on effort and even at rest, œdema present, systolic murmur at the apex of the heart, enlargement of the liver, left pleural effusion.

P.M.—The heart weighed $19\frac{1}{2}$ oz., adherent pericardium, dilatation of mitral valve, infarction of lung; each kidney weighed 7 oz., described as chronic interstitial nephritis, the surfaces were red and granular.

Case 45 was admitted for cardialgia, palpitation, dyspnœa and dropsy, cyan-

osis, irregular pulse, apical systolic murmur, enlargement of the liver : sudden and unexpected death.

P.M.—Slight atheroma in the aortic and mitral flaps, otherwise heart hyperpiesic in type : right kidney weighed 5½ oz., left kidney, 6 oz., surfaces finely granular ; described as chronic interstitial nephritis. Heart weight, 17½ oz.

This group of ten cases, with one or two exceptions already referred to, presented the features so frequently associated with cardiac failure : the curious phenomenon of attacks of dyspnœa, at different times described as examples of Cheyne-Stokes breathing, is met with clinically in a variety of diseases, including intracranial disease, cases of cardiac disease, and cases of kidney disease ; it has been shown that very probably this phenomenon occurring in cardiac and in renal disease, may be due to a toxæmia, the particular result of which is a reduction of the alkalinity of the blood. This provides a reason for taking exception to the view that cases who present the phenomenon of periodic breathing owe it to kidney disorder. One of this last group of cases, No. 45, appears to be an example of almost pure Hyperpiesia, the immediate cause of death being apparently due to cardiac failure ; there does not appear to be sufficient reason for thinking that the condition of the kidneys had caused death, nor was there any sign of recent terminal infection ; the irregular pulse observed during life encouraged the view that the conducting fibres of the heart were involved in some undefined toxic process, for the report by the pathologist stated that there was no fibrosis of the cardiac muscle. It will be observed that in this case the heart weighed 17½ oz., and that though the total kidney weight was 11½ oz., they were described as being examples of chronic interstitial nephritis, that the capsules were adherent and thickened, that the surfaces were finely granular, and small cysts were present : clinically the case did not present evidence of kidney disease.

The remaining nine cases of this group show heart weights varying from 15 to 26 oz., and though part of this increase in weight was due to hyperpiesis, another part, impossible to determine in amount, was due to various valvular abnormalities, except Case 11. Amongst these nine cases there was noticed the now familiar variability in the configuration and other features of the kidneys, and though the kidneys in each of these nine cases were so altered as to justify the application of the term " granular kidney " or " chronic interstitial nephritis," to these organs in each case, in only one case was the total kidney weight less than normal total kidney weight. In Case 3 it was 9 oz. ; Case 23, 12½ oz. ; Case 29, 8 oz. ; Case 36, 11 oz. ; in Cases 40 and 41, 11½ oz. ; in Case 44, 14 oz. ; and in Case 42, 19 oz. In Case 11 the weight was 7½ oz. No doubt in some of these cases the kidneys shared in the engorgement, which as a result of cardiac failure also revealed itself in the " nutmeg " livers of some of the cases.

Turning to the microscopic appearance of the kidneys of Case 45, Mr. Lawrence reported that only slight glomerulo-tubular atrophy was found, and only 3 per cent. of the Malpighian corpuscles were destroyed ; small areas of tubular atrophy, accompanied by fibrosis, were present, but were sparse. Again the main bulk of the tubular epithelium was swollen and undergoing granular destruction,

although the kidneys were removed shortly after death and at once injected; in this case there were no coarse signs at the post-mortem examination of any terminal infection, so that the cause for the parenchymatous degeneration can only be a matter of speculation, being either some terminal infection which was undiscoverable, or being some form of toxæmia at present unidentified. The kidneys in this case appeared to be congested, as were the lungs and liver, and there was only slight intimal change in the various arteries of the kidney.

The study of this fourth group shows, therefore, that death may occur in Hyperpiesia as in cases of disease of the myocardium, endocardium or pericardium, from cardiac failure, the presumption being, as in these cases, that cardiac failure was due to toxæmia of an infective or non-infective (undetermined) nature.

ANALYSIS OF THE RECORDS OF THE CASES IN WHOM AT POST-MORTEM EXAMINATION CARCINOMA OF SOME PART OF THE BODY WAS FOUND AND CAUSED DEATH WHOLLY OR IN PART (GROUP 5)

Reference has already been made to Case 8, in whom carcinoma of the rectum was found; but it was pointed out that death was due to "uræmia" and not to carcinoma, and so the case has been included in the first group. Case 48 was also included in the first group as a case of death from "uræmia"; but in this case the kidney disease which had been produced was dependent upon carcinoma of the bladder, which involved the ureteral orifices. There still remain four other cases in whom at the post-mortem examination carcinoma was found.

In CASE 12 the history suggested cardiac disorder, because the patient was short of breath and developed dropsy, the impulse of the heart was found external to the nipple, nycturia was present, but albuminuria occurred only twice out of the seven occasions on which the urine was examined. After some improvement and disappearance of the dropsy he was noticed to be becoming anæmic: he suddenly developed severe hæmatemesis, which continued till death on the following day.

P.M.—The heart was of the hyperpiesic type and weighed 18 oz.: the kidneys weighed 5 oz. each, the surface was slightly granular, and the organs were described as examples of early cirrhosis: the kidneys were not injected immediately after death, and were said microscopically to show slight glomerulo-tubular atrophy: there was a little fibrosis: 85 per cent. of the Malpighian corpuscles appeared to be normal: there was only slight intimal sclerosis of the arteries. The hæmatemesis was due to cancer of the stomach.

CASE 13 was admitted to hospital for an empyema which had developed as a result of carcinoma of the œsophagus: the patient died of starvation and septicæmia. Clinically the heart showed hyperpiesic characters, and the brachial vessels were found to be tortuous: albumen was always absent from the urine.

P.M.—The heart weighed 13 oz. and was of the hyperpiesic type: red granular kidneys, each weighing 6 oz.: carcinoma of the œsophagus and left empyema. Microscopically slight glomerulo-tubular atrophy: 7 per cent. of the Malpighian

corpuscles were destroyed: slight amount of fibrosis: arteries very little altered.

Case 30 was admitted for symptoms which were very suggestive of carcinoma of the stomach, vomiting being the chief feature: this became fæcal in character shortly after admission: the patient died of inanition: there were hyperpiesic changes in the heart and arteries: albumen was absent on the four occasions on which it was looked for.

P.M.—The heart weighed 18 oz., left ventricle greatly hypertrophied: no valvular defects: kidneys weighed 4 oz. each, and presented all the characters of a red granular kidney. Microscopically there was considerable glomerulo-tubular atrophy: 24 per cent. of the Malpighian corpuscles were destroyed: the thickening of the intima of the arteries was considerable: cancer of stomach.

Case 37 was admitted for symptoms suggesting cardiac disease; but in addition her appetite was found to be defective and she was losing flesh: the heart revealed murmurs: the urine was examined twice and was found to be free from albumen and blood, though casts were found: there was albuminuric retinitis. The patient was found to have carcinoma cervicis and the temperature rose just before death and was dependent upon left-sided pneumonia.

P.M.—The heart was hypertrophied and weighed 18 oz., the increased weight being probably due to valvular defect as well as hyperpiesis: left-sided pneumonia and carcinoma of the cervix: the kidneys weighed $2\frac{1}{2}$ oz. each, and the surfaces were finely granular in some places and in other places showed numerous large irregular depressed areas: one kidney was injected shortly after death. The microscopic examination showed the destruction of 13 per cent. of the Malpighian corpuscles in the unscarred cortex and 100 per cent. in the scarred portion. With regard to the tubules, those belonging to the part of the kidney which was granular on the surface showed atrophy which was not universal, whereas the tubules in the scarred portion were almost all atrophied: fibrosis was absent in the scarred part of the kidney: some thickening of the intima was found in all the renal arteries, but was very marked in those of the scarred areas.

This group of cases gives further opportunity for studying the condition of the heart and kidneys in hyperpiesis, death having taken place from causes other than cardiac or renal failure, with the exception, perhaps, of Case 37, in whom mitral disease was present: the remaining three cases show the characteristic hyperpiesic heart, the weights varying from 13 to 18 oz.: the kidneys in Case 12 showed only slight early cirrhosis, and the total weight was 10 oz., whereas in Case 13, though the total weight of kidney substance was 12 oz., they were of the red granular type. In Case 30 red granular kidneys were present, and the total kidney weight was 8 oz. It is of interest to note that Case 37, in whom the total weight of the red granular kidneys was only 5 oz., *did not die of the renal inadequacy*: it looked as if the clinical manifestations, as already stated, were due to cardiac disorder of very moderate severity, and that death really resulted from the terminal infection—pneumonia occurring in a person who had carcinoma of the cervix.

ANALYSIS OF THE RECORDS OF CASES DYING OF APOPLEXY (GROUP 6)

CASE 6 has already been referred to under the first group of cases said to be "uræmic," the case being placed in that group because of the marked "uræmic" character of his illness, before apoplexy from cerebral hæmorrhage occurred.

CASE 43 also died from apoplexy, but again it was felt preferable to place his case in the first category rather than in this one, because of the probable "uræmic" nature of the fits from which he had previously suffered.

In addition to these two cases, CASE 34 was found to have died of a left meningeal hæmorrhage, 5 oz. of old brownish, breaking-down clot being found spread over the left side of the cerebrum. No fractured skull could be found to explain it: the patient had simply become unconscious three days before admission, and died in about a week: he had had practically no symptoms of ill-health up to ten days before the onset of the meningeal hæmorrhage; early optic neuritis: albuminuria, but no casts.

P.M.—Hyperpiesic heart, weighing 15 oz. Each kidney weighed 7 oz., and showed early and slight parenchymatous nephritis, very slight glomerulo-tubular atrophy, slight arterial disease, slight fibrosis.

CASE 50 was admitted to hospital comatose: a relative thought he had had a paralytic stroke a month or two previously: other than excessive alcoholism and marked irritability of temper, no further suggestive history could be obtained: there was evidence of cardio-vasculo-renal change: no casts or changes in the eyes.

P.M.—Right cerebral hæmorrhage (recent), right-sided pontine hæmorrhage (recent), and an old cerebral hæmorrhage in the right occipital lobe: heart hyperpiesic, weighing 13½ oz.: granular kidneys, each weighing 4 oz.: one kidney was injected shortly after death: 50 per cent. of the Malpighian corpuscles were atrophied: extreme tubular atrophy: fibrosis: moderate thickening of the inner coat of the arteries of the kidneys, and considerable thickening of the middle coat of the same vessels.

These two cases of death, the one from meningeal and the other from intracerebral hæmorrhage, show two conditions of the kidney which are very different. In Case 34 there was comparatively little change in the kidneys, and the total weight was 14 oz., whereas in Case 50 the total weight of the kidneys was normal namely 8 oz., and yet they were examples of granular kidney. In both cases there was evidence of the presence of Hyperpiesia, because the left ventricles were hypertrophied and the cardiac weight was increased, independent of valvular disease. Death was not due in Case 50 to the condition of the kidneys, although only 50 per cent. of the Malpighian corpuscles were normal.

GROUP 7 INCLUDED ONE CASE OF SUDDEN AND UNEXPECTED DEATH—CASE 2

She had suffered for two years with shortness of breath and palpitation: there was an apical systolic murmur, albuminuria and albuminuric neuro-

retinitis : there was also dropsy and occasional fever during both visits to the hospital.

P.M.—The heart was found to be hyperpiesic, and both ventricles were dilated as well as hypertrophied : the mitral valve was thickened : the heart weight was 23 oz. : the kidneys weighed 7 and 7½ oz. respectively, and were congested : only 10 per cent. of the Malpighian corpuscles were destroyed : there was some tubular atrophy, with fibrosis, and slight thickening of the internal coat of the arteries of the kidneys. Presumably death had occurred from failure of the cardiac muscle ; during life the case presented features, even well-marked albuminuric retinitis, of grave kidney disease ; the pathological report on the kidneys described them as chronic Bright's disease, but microscopically there was only " slight glomerulo-tubular atrophy due probably to a past capsulitis."

HISTOLOGY

Mr. LAWRENCE contributes the following remarks, which are illustrated by his histological observations on the kidneys in this series of cases :

"RENAL ATROPHY

" The term ' Renal Atrophy ' is commonly used to denote a reduction of the renal substance from whatever pathological cause : thus the small and deformed

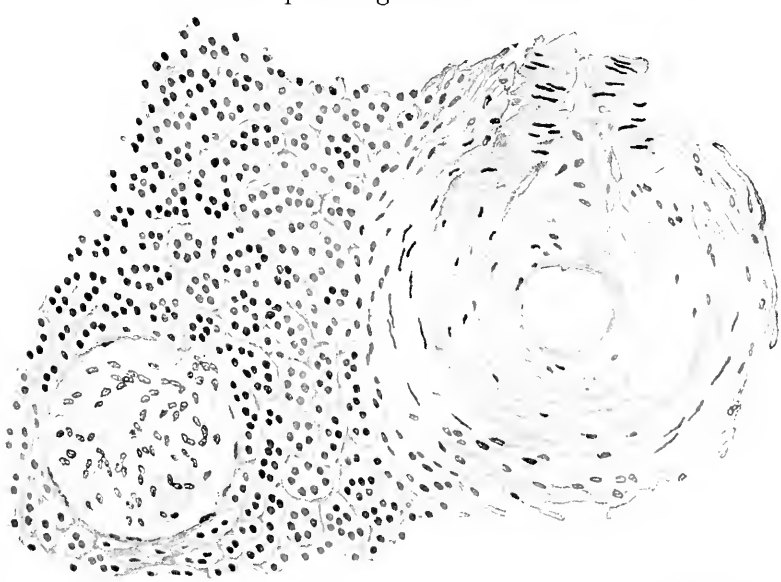


FIG. 2 (Case 4).—An endarteritic interlobular artery ; consequent tubular atrophy ; Malpighian corpuscle fairly normal, not atrophied : slight hyaline thickening of the intertubular tissue.

kidneys arising from congenital mal-development are spoken of as atrophic. Physiologically speaking, the name should be applied only to the anatomical changes associated with a lowered function of the cells, apart from other pathological changes in them, a diminution in the blood-supply being the usual cause.

"Renal Atrophy does not exist as a disease by itself, but is present in greater or less degree in many chronic affections of the kidneys. In the Red Granular Kidney, and in the Small Granular Kidney of Chronic Glomerular Parenchymatous Nephritis, it constitutes the most important part of the lesion, and these diseases would be more accurately denoted respectively as Vascular Atrophy of the kidney and Capsulitic Atrophy of the Kidney than by their present names.

"The anatomical changes which characterise atrophy in the physiological sense of the term (see Figs. 2 and 3) are found both in the epithelium of the tubules and of Bowman's capsule. In the earlier stages there is a mere reduction in the size of the cell; in later stages the protoplasm loses its granules and becomes perfectly clear, while from the continued reduction in size the cell loses its pyramidal form and becomes cubical. In still more marked degree, the protoplasm is hardly recognisable, and the deeply stained and somewhat shrunken nucleus gives the cell somewhat the appearance of a lymphocyte. Ultimately many of the cells disappear entirely, as the existence of tubules containing only one or two cells in the cross section sufficiently proves (Figs. 3 and 4).

FIG. 3 (Case 8).—An endarteritic interlobular artery; consequent tubular and corpuscular atrophy—tubules small, protoplasm of renal epithelium reduced to a minimum, nuclei closely placed; corpuscles small, epithelium largely disappeared.

"While these changes are proceeding in the renal cells, the intertubular tissue remains unaltered: interstitial fibrosis may be superadded, but it is frequently absent, and is not an essential part of the atrophic process. In consequence of these changes the diameter of the tubules is reduced, the lumen is narrowed or obliterated, provided no obstruction is present in the lower portions of the tubes, and the affected portion of the cortex undergoes a corresponding diminution in bulk. Where isolated glomerulo-tubular systems, or groups of such systems, escape the atrophic change, these will appear as rounded granules on the surface of the kidney, projecting above the level of the atrophic areas: otherwise the area appears as a smooth depression.

"Pathological glomerulo-tubular atrophy originates mainly in three ways: by diminution of the blood-supply (ischæmia) through changes in the arteries or glomerular capillaries; by obstruction in the course of the tubules or lower down in the urinary channels; and by shrinking of the tissues in cirrhosis of the organ. These differences furnish a basis of classification into sub-classes:

"I. Ischæmic Atrophy

"(*a*) From Occlusive Vascular Disease (Figs. 2, 3, 4, 5 and 6).—Here the arrest of blood-supply upon which the atrophy depends is primarily due to disease of the vessels. The arterial disease may affect mainly the large vessels (arciform arteries), in which case extreme reduction of the lumina is necessary to produce any marked atrophy of the cortex. Or the interlobular and afferent arteries may be the main seat of obstruction and then the cortex is more readily affected. Thirdly, the glomerular capillaries may be the principal seat of disease, usually in the form of hyaline degeneration of the tuft (Figs. 4 and 6). When

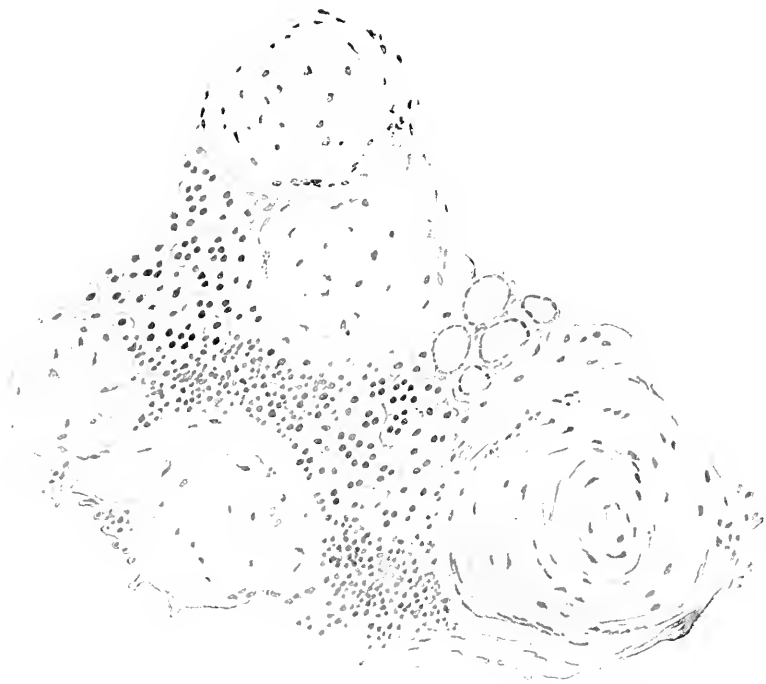


Fig. 4 (Case 15).—Endarteritis of interlobular and afferent arteries. Hyaline degeneration of the corpuscles.

the obstruction is extra-glomerular the Malpighian corpuscle is not necessarily destroyed, but if the vascular obstruction is extreme it undergoes simple atrophy analogous to that suffered by the tubules (Fig. 3). Thrombosis within the capillaries of the tuft leading to its necrosis (Fig. 5) often plays a part in determining the obstruction both in this variety of the disease and in some of the forms to be mentioned subsequently. The best example of Vascular Atrophy is the red Granular Kidney.

"The histological distinction between Simple Atrophy, Hyaline Degeneration and Necrosis of the glomerular tuft is not difficult when these conditions are found singly. The picture is complicated when they are combined and associated with Chronic Capsulitis.

"*Simple Atrophy of the Tuft* (Fig. 3).—This occurs when the small afferent vessels are *gradually* blocked. Changes occur analogous to those in the tubules: the epithelium loses much of its protoplasm, which becomes clear, and many of the cells disappear entirely; the capillaries appear to shrink, and the whole corpuscle is greatly reduced in size and becomes indistinct. The corpuscles shown in the figure are in an intermediate stage of atrophy: in more marked degree it is difficult

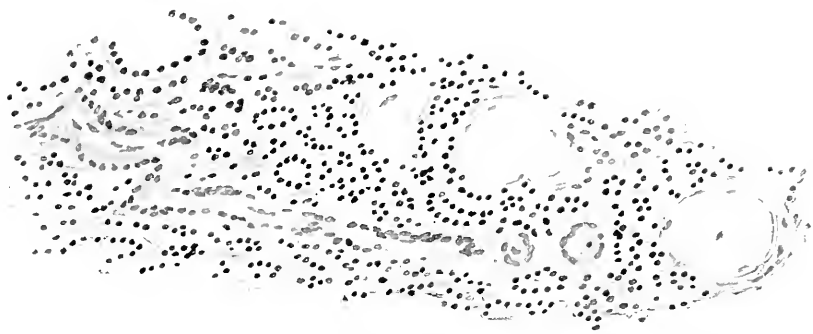


FIG. 5 (Case 33).—Endarteritis of afferent artery. Necrosis of the tufts probably through capillary thrombosis. Atrophy of the tubules, the result of the arterial disease.

to distinguish them from the surrounding atrophied tubules, and many of them evidently disappear. It is often found in cases of contracted kidney that the number of glomeruli present in a microscopic section is much less than the loss of tubular substance would lead one to anticipate; the explanation is probably to be found in the disappearance of glomeruli by the process of simple atrophy.

FIG. 6 (Case 47).—Three stages in the atrophy of a Malpighian Corpuscle due to hyaline degeneration of the tuft. In the largest corpuscle there is also an organised capsulitis which, however, does not interfere with the hyaline effect. This kidney showed marked hyaline arterial disease. The tubules are atrophic.

"*Hyaline Degeneration of the Tuft* (Figs. 4 and 6).—A very different result follows when the atrophy is associated with hyaline degeneration: in this case the glomeruli persist and crowd the microscopic field, owing to the loss of intervening tubules. In advanced cases the tuft is composed of a mass of clear, highly refractile, firm material, in which the lumina of the capillaries appear to be embedded at relatively wide intervals; the capillaries,

in fact, are separated by stout hyaline trabeculæ, differing greatly in character from the delicate strands which normally separate them, such as are shown in Fig. 3. The atrophy which results from hyaline degeneration is *gradual* in development.

"*Necrosis of the Tuft* (Fig. 5).—This form of atrophy is produced when the afferent vessels are *suddenly* closed by thrombosis or embolus. It is readily distinguished from hyaline degeneration by the absence of the rigid hyaline trabeculæ present in all advanced cases of the latter condition, and from simple atrophy by the absence of the clearly defined and delicate fibrillæ that separate the capillary lumina. The whole tuft looks hazy, without sharp outline and without any clear details of structure in its substance. It often has a finely granular appearance, which is probably the result of thrombosis of the capillaries. Both Necrosis and Hyaline Degeneration may affect part of the tuft only, for instance a single capillary loop.

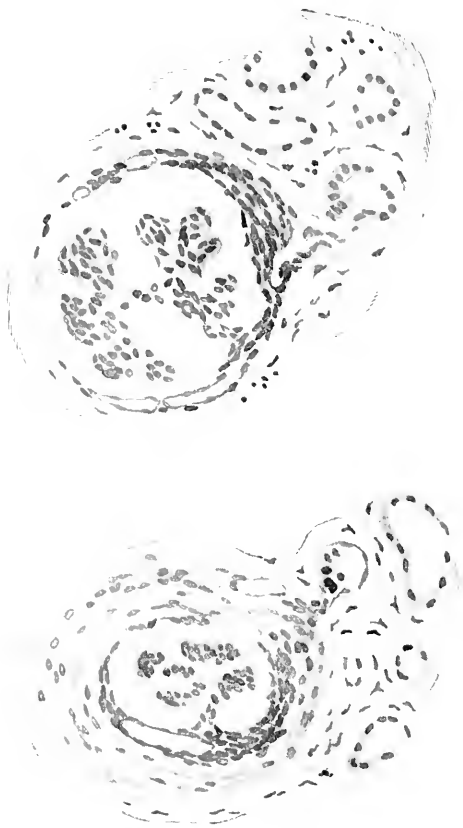


FIG. 7 (Case 6).—Proliferative capsulitis. In the lower figure organisation of the peripheral layers of the epithelium has occurred. There is no adhesion of the glomerular tufts.

"(*b*) CAPSULITIC ATROPHY (Figs. 7, 8A, 8B, 8C and 9).—Here the arrest of blood-supply upon which the atrophy depends is primarily due to inflammation of Bowman's capsule and consequent destruction of the glomerular tuft. The usual course of events appears to be that the capsulitis (Fig. 7), instead of resolving, terminates in adhesion of the capsule and destruction of the tuft by extension of fibrosis into its substance. In proliferative capsulitis the destruction of the tuft is preceded by its compression by the mass of organised epithelium (Fig. 9), and indications of the process are often found in the form of an unequal or semilunar thickening within the shrunken capsule (Fig. 9). That destruction of the tuft may result from capsulitis is often sufficiently obvious (Fig. 9), but in cases where proliferation and organisation of the capsular adhesions are absent and the tuft becomes directly adherent to the capsule (Figs. 8A, 8B and 8C), the resulting change bears a general resemblance to the Hyaline Degeneration seen in Fig. 4. The more highly refractile appearance of the hyaline change, and the fibrillated character of the capsulitic fibrosis, serve to distinguish the two as a rule. The best

evidence of the distinction, however, is seen in early stages, when the tuft is only partly affected; in adhesive capsulitis a patch of fibrous tissue can be seen extending into the tuft at the point of adhesion, while in Hyaline Degeneration the process begins as a highly refractile thickening of the capillary walls.

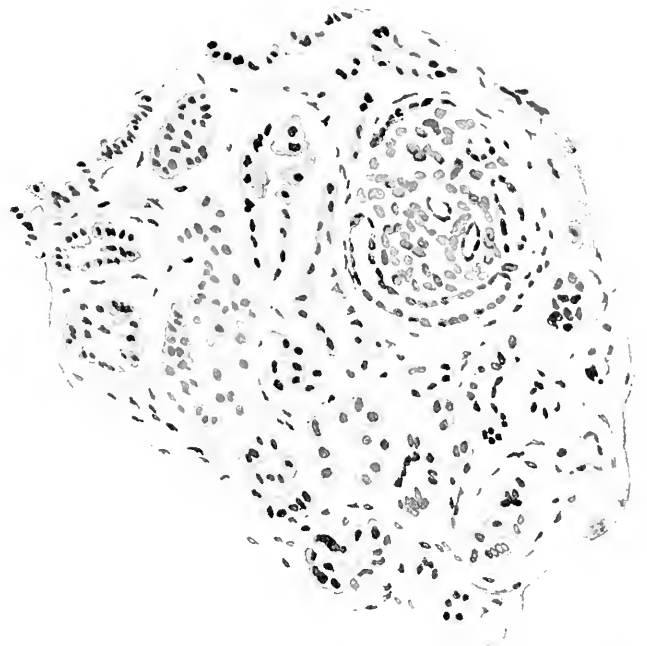


FIG. 8A (Case 22).—Non-proliferative glomerulo-tubular nephritis, showing direct adhesion of the glomerular tuft to the capsule.

"It is impossible to state exactly what degree of narrowing of a vessel is necessary to cause atrophy of the cortical tubules, and there is the same difficulty in regard to capsulitic atrophy. Probably a certain proportion of the corpuscles of a given area must undergo destruction before renal atrophy is produced, while the destruction of an isolated corpuscle would have little or no effect and cause no renal atrophy. Many typical examples of granular kidney are of this nature, and are therefore related to parenchymatous nephritis.

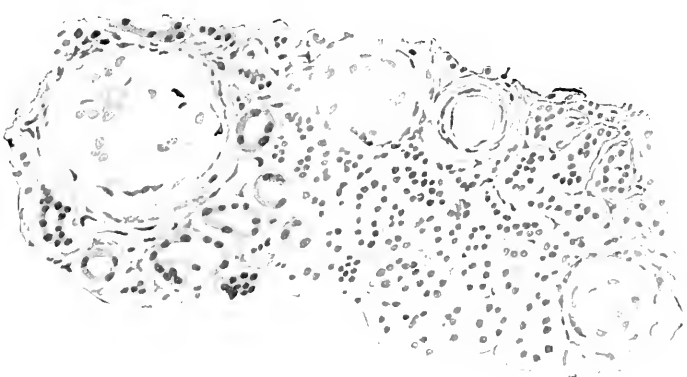


FIG. 8B (Case 22).—Destruction of the glomerular tufts from non-proliferative capsulitis. In part of the section there is marked tubular atrophy. There was very trifling disease of the arteries.

"The Secondary Contracted Kidney of Tubular Nephritis, in cases where the Malpighian corpuscles are not extensively destroyed and the arteries are free from disease, belongs to a different category, and is usually distinguishable macroscopically from the Small Granular Kidney of Capsulitic Atrophy. In the Secondary Contracted Kidney the shrinking is probably due mainly to loss of renal epithelium resulting from degeneration and desquamation, and possibly from some degree

FIG. 8C (Case 22). — Non-proliferative glomerulo-tubular nephritis. Great reduction in the tubular tissue, due probably to the combined effect of desquamative-nephritis and atrophy from destruction of the tuft.

of contraction, consequent on the accompanying fibrosis (Figs. 8A, 8B and 8C).

"Capsulitic Atrophy may occur alone, but it is also superadded to other forms; for instance, a Vascular Atrophy is frequently intensified by association with it. Capsulitic Atrophy is followed by atrophy of the tubules, the latter form of atrophy being sometimes spoken of as the atrophy of inactivity.

"II. OBSTRUCTIVE ATROPHY

"Hydronephrosis affords one of the best and most familiar examples of renal atrophy, and is probably due to diminution of the blood-supply by the pressure of the retained urine. Owing to the liability of such

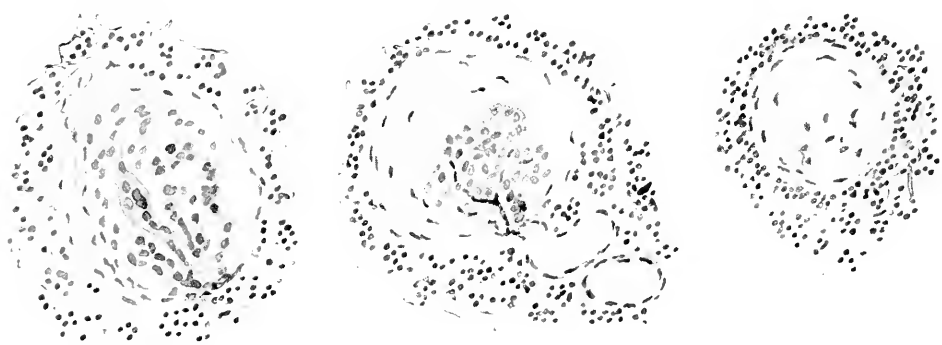


FIG. 9 (Case 32).—Progressive destruction of the glomerular tuft from proliferative capsulitis. Marked atrophy of the tubules. There was in this case a widely distributed disease of the arteries without marked narrowing of their lumina.

a kidney to infection it is frequently associated with chronic interstitial nephritis.

"III. CIRRHOTIC ATROPHY

"The presence of intertubular fibrosis or chronic interstitial nephritis is by no means constant in tubular atrophy of the kidney (Figs. 3 and 4). It is, however, often present, and sometimes in marked degree, especially in the later stages of Red Granular Kidney, and in such cases it intensifies the atrophic process, owing to its constricting action. The best instances of Cirrhotic Atrophy are to be found

in the so-called Red Granular Kidney, in which it is combined with endarteritis and in the secondary induration which results from irritation of the renal pelvis, as in cases of calculus, where without any marked suppuration the renal substance contracts down on the stone. Cases of Primary Interstitial Nephritis independent of arterial disease have been described, but they appear to be of extreme rarity, and the same may be said of the so-called Cyanotic Atrophy, which is said to result from long-standing venous congestion.

"It is possible that other and less marked forms of atrophy exist, such as Senile (Case 18) and Toxic (alcoholic) Atrophy (Case 27).[1]

"As regards the course of Renal Atrophy, it is evident that when a glomerulo-tubular system has been destroyed the condition is stationary and irremediable. But regarding the organ as a whole, consisting as it does of innumerable glomerulo-tubular systems, the condition may be progressive. Different glomerulo-tubular systems may be successively attacked and the atrophic process extend through the organ.

"Besides capsulitis there is tubulitis, but it is not so easy to detect the latter, because there is no special visible proliferation as in the case of capsulitis. Tubular atrophy may result from capsulitis because the capillaries of the glomerular tuft become obstructed as the result of the capsulitis.

"Simple atrophy of the tuft is not a special form of atrophy, dependent upon some unknown process: it is brought about by the gradual reduction of the blood-supply to the glomeruli and tubules without actually cutting off the blood-supply, *e.g.* if the afferent vessel is narrowed, the glomerular tuft will atrophy, as well as the capsule and *pari passu*, the tubular epithelium which is supplied with blood by the efferent vessels of the glomerulus will also undergo simple atrophy.

"Necrosis of the tuft is produced by suddenly completely cutting off the blood-supply by arterial or capillary occlusion.

"Hyaline Degeneration of the tuft of the Malpighian corpuscle is again the result of a toxic body arriving by the blood-stream which leads to the deposit of hyaline material in the walls of the capillaries in scattered masses, or quite diffusely.

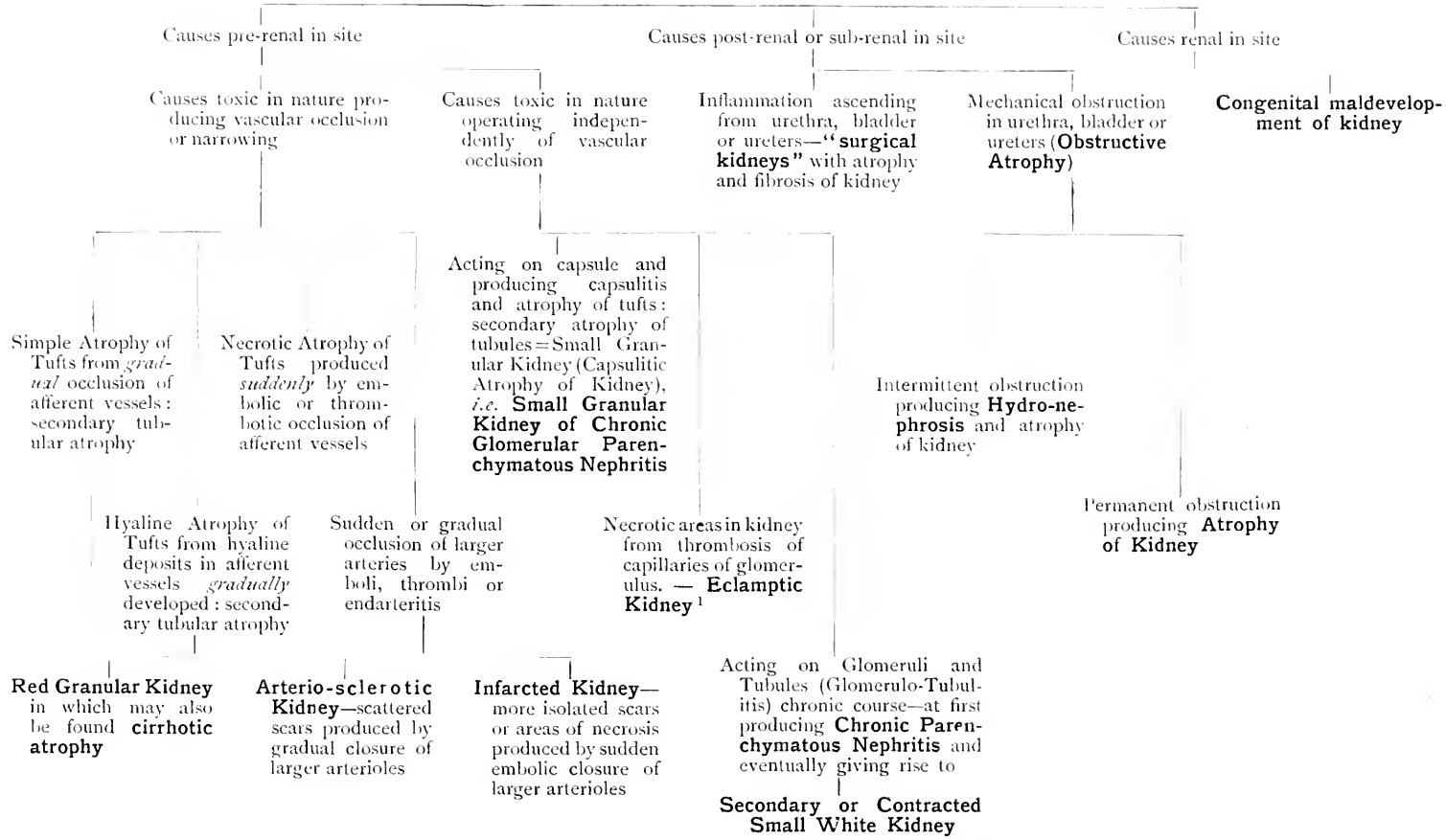
"Granular change and cloudy swelling of the tubular epithelium, when found in the kidneys, may be the result of a recent acute infection, or may be the result of a chronic infection that has been in existence some time, or may be the result of autolysis.

"The Large White Kidney is a kidney in which some toxic body generated at a pre-renal site which only too often is undiscoverable, produces continuous degenerative changes in the glomeruli and tubules: it does not produce atrophy in all cases, because repair can keep pace with destruction, and there is no atrophy of corpuscles or tubules.

"The Secondary Small White Kidney, that is, the Contracted White Kidney, on the contrary, shows that the above-mentioned agencies have at last defeated

[1] See Note, p. 75.

SCHEME SHOWING THE VARIOUS FORMS OF KIDNEY DISFIGURATION RESULTING FROM PATHOLOGICAL ATROPHY OF THE SUBSTANCE OF THE KIDNEY FROM VARIOUS CAUSES



[1] Probably the thrombosis is only a part effect—both it and the necrosis resulting from the unknown toxic cause of Eclampsia, similar changes being produced in the liver.

the power of repair; the glomeruli then atrophy and the tubules as well, the latter from the primary effect of the toxic agent, in part, and as a result of the corpuscular atrophy in another part (atrophy of inactivity).

"The Primary Small White Granular Kidney is probably due to capsulitis, which is followed by atrophy of the tuft, and as sequence of this latter, by tubular atrophy.

"The Red Granular Kidney is entirely due to occlusive endarteritis of the small arterioles of the kidney, of the afferent vessels of the tuft, and of the capillaries of the tuft. The Scarred Kidney, *i.e.* the Arterio-Sclerotic Kidney, is due to occlusive endarteritis of the larger interlobular arteries or arteriæ arciformes.

"RENAL HYPERTROPHY

"1. The atrophic processes described are commonly associated with compensatory hypertrophy in the unaffected portions of the renal substance. This is evidenced more especially by the enlargement of the corpuscles seen on microscopic examination, but also by the production of granules on the surface of the kidney, which although in the main caused by shrinking of the surrounding tissue are in some instances due to hypertrophy, since they may be present in cases where the atrophy is slight and in kidneys but little reduced in size.

"2. A less recognised form of hypertrophy is exemplified by two cases of the present series (Cases 42 and 46). The kidneys are practically free from any pathological changes when examined microscopically, and greatly exceed their normal weight (the kidneys weighing $9\frac{1}{2}$ oz. each in one and 10 oz. each in the other one). In Case 46 the total weight of renal substance amounted to two and a half times that of the healthy individual. Such an increase is outside the limits of normal variation, and since it is not compensatory to destructive processes in the kidneys themselves, it would appear to be due to some at present unknown influence.

"3. From one point of view it is possible to regard certain cases of Chronic Parenchymatous Nephritis as hypertrophic, namely, those in which proliferation of the epithelium occurs. The proliferation (Fig. 7) when present is always evident in the capsule of Bowman. In the tubules it is only occasionally evident, though possibly it may be present in the form of an elongation of the tubules, the epithelium retaining its normal arrangement in a single layer, and thus appearing to be unaltered on microscopic examination. The great enlargement of the kidney in many cases of parenchymatous nephritis has been ascribed to œdema, increase in the interstitial tissue and swelling of the epithelium; but these may be insufficiently marked to account for the increase in the size, and it is sometimes difficult to avoid the conclusion that the tubules have enlarged by elongation. It has been customary to regard the epithelial proliferation as due to a catarrhal inflammation, but there is often a notable absence of leucocytic exudation, and some recent observers have discarded the view that the change is inflammatory, and have substituted the term 'Nephrosis' for 'Nephritis.' If this view is correct the epithelial proliferation must be of the nature of hypertrophy."

ANALYSIS OF THE MICROSCOPIC CHANGES MET WITH IN THE KIDNEYS OF TWENTY-SIX OF THE FORTY-SEVEN CASES IN WHOM A KIDNEY WAS INJECTED WITH PRESERVATIVE FLUID SHORTLY AFTER DEATH, *i.e.* BEFORE POST-MORTEM AUTOLYTIC CHANGES COULD HAVE BEGUN.

The cases under consideration are Nos. 1, 3, 4, 5, 7, 8, 9, 10, 14, 20, 22, 29, 30, 31, 32, 33, 35, 37, 40, 41, 42, 43, 45, 48, 49, 50. Naked-eye examination of the kidneys resulted in various names being applied to these organs.

Red Granular Kidney, Nos. 3, 4, 7, 20, 22, 29, 30, 49	8 cases.
Granular Kidney, Nos. 1, 8, 9 (R), 10, 32 (R), 33, 37, 50	8 ,,
Renal Sclerosis, Nos. 5, 43, 48 (L)	3 ,,
Fibroid Kidney, No. 14	1 ,,
Chronic Interstitial Nephritis, Nos. 31, 41, 42, 45	4 ,,
Cirrhotic Kidney, No. 40	1 ,,
Atrophied Kidney, No. 32 (L)	1 ,,
Hydronephrotic Kidney, Nos. 9 (L), 48 (R marked, L slight)	2 ,,
Scarred Kidney, Nos. 20, 37	2 ,,
Chronic Parenchymatous Nephritis, No. 35	1 ,,

THE RED GRANULAR KIDNEYS

These varied in total weight from 5 oz. (Case 7) to 9 oz. (Nos. 3 and 20). Only three cases (Nos. 4, 7 and 22) showed less total weight than normal kidneys, namely, 8 oz. The functional capacity of these kidneys may be roughly compared by noting the percentage of glomeruli which were healthy, or if altered were capable of functioning. It is impracticable to refer to the tubules as a measure of functional capacity because of the impossibility of fixing the individuality of each tubule: lowered function of the tubules would at least be as marked as that of the glomeruli when the atrophy of the latter was due to toxic causes not producing arterial or capillary occlusion or wasting; it would outstrip the lowered function of the glomeruli when cloudy swelling and granular degeneration affected the epithelium of the tubules. The percentages of normal glomeruli varied from 30 per cent. in cases numbered 3 and 22, to 93 per cent. in Case No. 4. How little parallelism there is between total weight of kidney substance and percentage of normal glomeruli is shown by the fact that Case 3, with a total weight of 9 oz., showed 30 per cent. normal glomeruli, and Case 20 of the same total weight showed 88 per cent. normal glomeruli, and Cases 29, 30 and 49 of almost the same total weights showed respectively 74 per cent., 76 per cent. and 54 per cent. of normal glomeruli.

It is clear therefore that the total weights of red granular kidneys give no clue to the percentage of normal glomeruli present. If an effort be made to fix the difference of the kidneys in these cases by reference to some common microscopic change, qualitative as well as quantitative, the following features are observable:

Case	3,	the chief	cause	of change	was hyaline degeneration of the glomerular tufts.
Case	4,	,,	,,	,,	,, atrophy of the tubules from occlusive arterial disease.
Case	7,	,,	,,	,,	,, the same as in Case 4.
Case	20,	,,	,,	,,	,, necrosis of the tufts from some toxic cause—(?) terminal infection.
Case	22,	,,	,,	,,	,, capsulitis and consecutive atrophy of the tubules, to which was added chronic tubular nephritis, probably due to infection.
Case	29,	,,	,,	,,	,, the same as in Case 22.
Case	30,	,,	,,	,,	,, capsulitis.
Case	49,	,,	,,	,,	,, the same as in Cases 22 and 29.

It is thus clear that there is no common qualitative change which could account for the naked-eye similarity of these organs ; the causes ranging from alteration of the capillaries or arteries from essential vascular disease as in Cases 3, 4 and 7, to purely toxic causes which do not produce vascular disease as in Case 20, to toxic causes which have eventuated in capsulitis and consecutive atrophy of glomeruli and tubules as in Cases 22, 29, 30 and 49.

The interesting point is brought out that if Red Granular Kidneys are due to occlusive disease of the capillaries and arterioles of the kidney, five of these cases had been wrongly named, for the atrophy was dependent upon primary toxic parenchymatous change independent of vascular disease.

Retinitis was found in all three of the cases in which vascular changes were the chief causes of atrophy of the glomeruli and tubules, namely, in Cases 3, 4 and 7, but it was also present in Case 22, in whom atrophy was due to capsulitis and the vascular change was slight : no retinitis was found in three of the toxic cases, Nos. 20, 29 and 49 : there was no report in Case 30. Purpura was reported as present in only three cases, Nos. 4, 7 and 22, and in Cases 7 and 22 hæmorrhages were also found in the retinæ. In each of these cases terminal infection had occurred. Terminal infection was present in all cases except 29 and 30, and in neither of these last two cases were there reports on purpura or retinal hæmorrhages. There is some support therefore for the view that albuminuric retinitis is a more common feature in those cases in which renal atrophy is due to vascular disease than in those where it is due to toxic causes which operate on the parenchyma of the kidney, and that purpura and retinal changes are possibly expressive of infective processes.

The nature of the cause of death in these eight cases is of special interest, "uræmia" is given as the most likely cause of death in Cases 4, 7, 22 and 49, that is, in cases in which the total kidney substance weighed respectively 6 oz., 5 oz., 6 oz. and 8½ oz., and the glomerular atrophy was 7 per cent., 34 per cent., 70 per cent. and 46 per cent., the atrophy in Case 4 being due to arterial occlusion, and in Cases 22 and 49 to capsulitis with added chronic tubular nephritis.

It is clear that " uræmia " is not an expression of diminution of total weight of kidney substance, or to loss of glomeruli and of the associated tubules, or to vascular as compared to toxic, non-vascular causes of atrophy.

It is a striking fact that all the cases of "uræmia" showed well-marked terminal infection.

The cause of death in Case 30 was carcinoma of the stomach, and terminal infection and "uræmia" were absent.

The cause of death in Case 29 was said to be cardiac failure, but purulent bronchitis was also present. Cardiac failure caused death in Case 3, but there was terminal infection as well: "uræmia" did not occur, although the normal glomeruli only numbered 30 per cent.

The cause of death in Case 20 was simply terminal infection, the kidneys weighing 9 oz., and the normal glomeruli being 88 per cent.

This preliminary study of the histology of the eight kidneys which to the naked-eye appeared to be examples of Red Granular Kidney necessitates complete loss of confidence in such rough descriptions, for there was not found in these kidneys even a rough agreement in the histological findings—some were evidently the result of occlusive disease of the smaller arterioles, or of the glomerular tufts; others were clearly examples of primary disease of the parenchyma of the kidneys, and in some this latter change was dual in character—the change in part being due to a chronic structural alteration of the glomeruli and in part to a recent more acute process operating on the tubular epithelium. Nor was there any mode of death expressive of kidney inefficiency common to them; leaving out Case 30, in whom death was due to carcinoma of the stomach, of the remainder, four deaths were attributable to "uræmia" and two to cardiac failure, judging by the clinical manifestations. A most surprising common feature of the seven remaining cases as established by post-mortem was the existence of terminal infection, which was more or less suspected during life and appeared to be the sole cause of death in Case 20.

It would therefore seem more to the point to examine the whole of the twenty-six cases from the point of view of correlating the clinical manifestations with the histological pictures, careful attention being paid to what in the past has been spoken of as "uræmia," with the view of endeavouring to clear up some of the contradictions and shortcomings that cling to the use of this term. Clinicians have already been found to load "uræmia" with features so broad that there exist types of "uræmia" of such divergent characteristics as the cardiac, the respiratory, the nervous, the gastro-intestinal and other forms.

The compilation of Table III. has been difficult. The first heading is that of the "Clinical Evidence of Disorder of the Kidneys." It might be thought that the matter could have been simplified by stating whether each case was "uræmic" or not in the acute or chronic sense, or as already mentioned in accordance with the particular system whose ordinary functions have been rendered imperfect. As this study, however, includes a close examination of the kidneys in each case, *i.e.* of *the* organs mostly concerned in the development of "uræmia" according to the accepted ideas of how "uræmia" originates, the

TABLE III.—SHOWING DETAILS OF THE KIDNEY CHANGE IN TWENTY-SIX CASES, THE KIDNEYS BEING INJECTED BEFORE AUTOLYSIS COULD HAVE OCCURRED

No. of Case.	Clinical Evidence of Disorder of Kidneys.					Microscopic Evidence of Functional Capacity of		Cause of Parenchymatous Atrophy.		Recent or Terminal Tubular Degeneration.	Clinical Cause of Death.	Terminal Infection (found at P.M.).
	Non-obstructive Suppression of Urine.	Albuminuria. Constant.	Albuminuria. Occasional.	Retinal Change.	Dropsy or Effusion.	Glomeruli.	Tubules.	Ischæmic or Vascular.	Toxic Non-vascular.			
1	+	+		o	o	Few	Few	+	o	+	Anuria (? Uræmia)	o
3	o	+		+ (A.R.)	+	30 per cent.	,,	+	o	o	? Cardiac failure	Pericarditis
4	o	+		+ (A.R.)	o	93 ,,	Many	+	Slight capsulitis	o	Uræmia	Pericarditis, pleurisy, broncho-pneumonia
5	o	+		No report	+	98 ,,	Few	o	,,	+	,,	Erysipelas
7	o	+		+ (A.R.)	o	66 ,,	,,	+	Capsulitis	o	,,	Pericarditis, broncho-pneumonia
8	o		+	+ (A.R.)	+	50 ,,	,,	+	,,	+	,,	Pericarditis
9	o	+		No report	o	85 ,,	,,	o	,, (15)	+	Terminal infection	Pericarditis, empyema
10	o	+		No report	o	50 ,,	,,	+ (non-occlusive)	,,	o	,,	Pneumonia
14	+	+		+ (A.R.)	o	70 ,,	,,	+	,,	o	Uræmia	Pericarditis, endo-carditis, bronchitis
20	o		+	o	+	88 ,,	Many	Slight	Necrosis of tufts	+	Terminal infection	Empyema
22	+		o	+ (A.R.)	o ϕ	30 ,,	Few	,,	Capsulitis	+	Uræmia	Pneumonia
29	o		+	o	+ ϕ	74 ,,	,,	o	,,	+	Cardiac failure	Purulent bronchitis
30	o		+	No report	o	76 ,,	Many	o	,,	o	Carcinoma of stomach	o
31	o		+	+ (A.R.)	+	1–2 ,,	Few	Slight	,,	+	Terminal infection	Cellulitis of face
32	o	+		+ (A.R.)	+	R. 93 ,, / L. 5 ,,	,, / Almost none	,, / Much	,, / ,,	+ / o	? ,,	Meningitis
33	o	+		+ (A.R.)	+	40 ,,	Many	Slight	,,	o	,,	Pericarditis, pleurisy, pneumonia
35	o	+		Only hæmorrhage	+ ϕ	90 ,,	,,	,,	,,	o	Uræmia	Pneumonia
37	o	o	o	+ (A.R.)	+ ϕ	87 ,,	Few	,,	,,	+	Carcinoma cervicis (? Terminal infection)	Pneumonia
40	o	+		No report	+	95 ,,	,,	,,	,,	+	? Cardiac failure	Pleurisy and pneumonia
41	o		+	o	+ ϕ	84 ,,	,,	,,	,,	+	,,	Cellulitis of lip
42	o	+		+ (A.R.)	+	90 ,,	,,	,,	,,	+	Cardiac failure	Pleurisy
43	o	+		No report	+ ϕ	95 ,,	,,	o	,,	+	Cerebral hæmorrhage	o
45	o		+	No report	+ ϕ	97 ,,	,,	o	,,	+	Cardiac failure	o
48	o	+		o	o	L. 90 ,, / R. (Hydro-nephrosis)	Many	o	,, / Hydro-nephrotic atrophy	o	Uræmia (from Carcinoma of Bladder)	o
49	o	+		o	+	54 per cent.	Few	Definite	Capsulitis	+	? Uræma?, septicæmia	Pleurisy and cellulitis of face
50	o	+		o	o	50 ,,	Very few	Slight	,,	o	Cerebral hæmorrhage	o

ϕ = Complicated by valvular disease of heart.

A. R. = Albuminuric retinitis.

chief symptoms and signs referable to these organs and their functions have been taken as criteria of the inefficiency of them. One very important one was whether plenty of urine was being passed. No doubt many of the cases showed a diminution of urine during attacks of vomiting or inability to take liquids in the last few hours of life, but only those have been noted as ones of suppression of urine in whom the clinical notes have made reference to the fact and in which the diminution amounted to almost complete suppression. There were but three cases in whom this symptom had occurred: Case 1 showed anuria, and a microscopic study of the kidney showed how natural it was that anuria should have occurred, for few healthy unatrophied or non-degenerated glomeruli or tubules existed. Case 14, a case of "chronic uræmia," ultimately died with suppression of urine: the remarkable fact is demonstrated by the microscope that 70 per cent. of the glomeruli, though altered, in many cases were capable of functioning, the epithelium of the capsule being normal: uræmia could not be attributable to their fault. But the effect of the capsulitis which accounted for the destruction of 30 per cent. of the glomeruli was to destroy the corresponding tubular epithelium, and the epithelium of almost all the remaining tubules was atrophied or rendered functionless by the marked vascular disease. It may be considered that "uræmia" had resulted from the inability of various crystalloids to escape by their normal channels—the tubules: it remains, however, an enigma why the watery part of the urine should have failed to pass, seeing that 70 per cent. of the corpuscles were capable of functioning! Case 22 also revealed signs and symptoms during life indicating "uræmia," and died with suppression of urine. In this case, as in Case 1, the microscopic examination of the kidneys gave many reasons for considering that the "uræmia" was due to loss of function of the parenchyma of the kidneys, for capsulitis had led to the destruction of 70 per cent. of the glomeruli and the associated tubules and to disorder of 30 per cent. more of the glomeruli, though these later were capable of functioning. Only a few healthy tubules existed, for those which had escaped atrophy from the capsulitis had been assailed by chronic tubular nephritis, which in turn may have been originated by the terminal infection.

In the remainder of the twenty-six cases, suppression of urine as a sign of renal inefficiency was absent, including Case 31, in whom only 1 to 2 per cent. of the capsules were normal and as few tubules!

Albuminuria in these cases is considered as being constantly or only occasionally present. In seventeen cases it was always present, but in some cases this meant but one or two examinations: in eight cases it was only occasionally found: in one case, No. 37, it was absent on the only two occasions it was looked for.

In Cases 1, 7, 14, 32, 35, 40, albumen was always found, as well as casts, indicating a certain "renal" origin for the albuminuria. In Cases 1, 7 and 14 the histological examination confirmed the opinion that the kidneys were grossly affected, as in all three the tubules were markedly affected and the capsules in about 100 per cent., 34 per cent. and 30 per cent. were atrophied in the respective cases. Cases 32 and 35 were complicated by the occurrence of hydronephrosis in

one and valvular deficiency of the heart in the other. Case 40, an uncomplicated one, showed albuminuria on the four occasions it was looked for and also casts, but it will be seen that 95 per cent. of the glomeruli and only a few of the tubules were normal. That widespread tubular disease and scanty glomerular atrophy may be associated with only occasional albuminuria, is shown in Cases 20, 41 and 45. The question therefore may well now be raised whether albuminuria in some of these cases was not purely functional, occurring or not independently of organic change in the parenchyma—a support for the belief in the harmlessness (so far as organic disease of the kidney is concerned) of functional albuminuria of adolescence.

It is thought that the albuminous escape through the kidneys is *via* the glomeruli. It is to be expected, therefore, that there would be some parallelism between the occurrence of albuminuria in these twenty-six cases and the glomerular disease present in each.

TABLE IV

CONSTANT ALBUMINURIA.		OCCASIONAL ALBUMINURIA.	
No. of Case.	Percentage of Functioning Glomeruli.	No. of Case.	Percentage of Functioning Glomeruli.
4 . . .	93	8 . . .	50
5 . . .	98		
9 . . .	85	22 . . .	30
40 . . .	95		
42 . . .	90	31 . . .	1–2

It will be seen, however, that there is no parallelism from the accompanying table (IV.), in which cases are tabulated who are free from such a complication as valvular disease of the heart which might be considered to be the cause of the albuminuria. Albuminuria was constantly present in Cases 4, 5, 9, 40 and 42, and yet the percentage of functioning glomeruli was found to range from 85 per cent. to 98 per cent.; on the other hand, in Cases 8, 22 and 31, albuminuria was not always present and yet the percentage of functioning glomeruli was much lower, ranging from 1 to 2 per cent. to 50 per cent. It is doubtful, therefore, that the physical state of the glomeruli as determined by the microscope gives any clue which may be relied upon in the explanation of the passage or not of albumen during life. No doubt it will be objected that the glomeruli may look normal and yet be in such a state of functional disturbance as to allow albumen to pass. If this is the case the position must be given up once for all that if albumen escape through the glomeruli the objective condition of these bodies is necessarily such as to account for the abnormality. It seems more reasonable to suppose that in all cases of albuminuria the causal fault is a something which may allow the glomeruli to appear to be normal, or to be gravely damaged, such agents being

brought to the glomeruli in sufficient strength and quantity to be capable of exerting a temporary and functional, or permanent objective disruptive effect. The examination of this series of cases has shown an extreme want of parallelism in the amount and character of the urine passed and the naked-eye appearance of the kidneys in each case; the microscopic examination leads to just as bewildering results, so that the writer is driven to the position of considering that *the actual physical state of the kidneys cannot be defined in a large proportion of cases by clinical examination*; as already shown, life may persist in slow disintegration of the kidney, as in Case 1, until almost the last few glomeruli and tubules remain, death being brought about by the accompaniments of a complete anuria and what is known as "uræmia," or "uræmia" may develop in individuals who have 96 per cent. of normal glomeruli, as in Case 24. Table IV. also is helpful in explaining the albuminuria of adolescence, for it shows that the occurrence of albumen may be connected with such widely different degrees of damage of the glomeruli. The albuminuria of adolescence in its temporary character, and in its curability by the removal of septic foci, seems to be another example of how albuminuria depends upon toxic bodies brought to the kidney by the blood-stream, and not necessarily from the organic change in the kidney itself. The glomerulo-tubular arrangement "leaks" albumen because the glomeruli are destroyed, or damaged temporarily by the toxic action of the contents of the abnormal blood.

A fourth alleged feature of renal inefficiency is the occurrence of dropsy and the transudation of serous effusion. That both are independent of almost complete atrophy of the glomeruli and atrophy and degeneration of all the tubules is well shown in Case 1, in whom there was neither dropsy nor effusion, and it is reasonable to suppose that it is dependent upon some pre-renal cause operating on the capillaries. Cases 3, 8, 31, 33 and 49 show very marked change in the glomeruli and tubules and also dropsy. In Case 1 the pre-renal cause could not have been a terminal infection, as there was none. The dropsy must be due to some unrecognised agent acting on the capillaries of the body: in Cases 3, 8, 31, 33 and 49 such cause may have been the terminal infection which was present in each of them.

Table III. gives an opportunity of showing the connection between albuminuria and albuminuric retinitis.

Albuminuric retinitis was present in Cases 3, 4, 7, 8, 14, 22, 31, 32, 33, 37 and 42. In some of these cases albumen was always present when looked for: in three cases (Nos. 8, 22 and 31) only occasionally. In one case (No. 37) in whom albumen was looked for on two occasions, it was absent. The anomaly of this last case and of those cases in whom albumen was only occasionally found has been met by the clinical rule that before it is assumed that albuminuria is absent in any case under examination, repeated examinations should be made, not only of casual samples, but of a sample taken from a twenty-four hours' collection, and by the observation that occasional appearance of albumen is commonly met with in cases in which the kidneys have undergone such serious changes as to result in the reduction in size, in increase of fibrosis, granularity of surface, etc. With such a rule and statement in mind the absence of albumen in Case 37 on both examinations,

and the occasional absence of albumen in two other cases, is of no moment, for it probably would have been found by more careful examination that albumen was at some time or other present. That there is something wrong, however, with such teaching is shown by the fact that in Case 14 albuminuric retinitis was found, and albuminuria was present on each of the twenty occasions it was looked for (as much as $\frac{1}{10}$th to $\frac{2}{3}$rds of the depth of the test tube), and yet each kidney weighed $6\frac{1}{4}$ oz., being enlarged, and 70 per cent. of the glomeruli were normal! Moreover, quite a number of cases have been described in whom there was diffuse disease of the parenchyma of the kidneys and yet no albuminuria.

Albuminuric retinitis is therefore not a guide to the naked-eye appearance and to the weight of the associated kidneys. Turning to the possibly safer appeal to the microscopic study of these kidneys, it would appear that there was some fibrosis of the organs in Case 14, and that the underlying microscopic causes of the atrophy of almost all the tubules was, for 30 per cent., capsulitis, and for almost all the remainder occlusive disease of the interlobular arteries. Arterio-capillary disease would therefore appear to have been established in this case as a cause for the albuminuric retinitis. But if it is insisted that microscopic examination of the kidneys alone can establish the true alliance of albuminuric retinitis, namely, with intra-renal arterio-capillary disease, then unfortunately for such belief, supported as it is by Cases 3 and 4, which show that intra-renal vascular disease (serious in Case 3 and slight in Case 4) is present as the only causative change in the kidneys, and by Cases 7 and 8, in which although capsulitis—a parenchymatous affection—is present, arterio-capillary disease is also present—Case 33 shows that albuminuric retinitis may be attended with but one marked change in the kidney, namely, capsulitis (in 60 per cent. of the glomeruli) with but slight arterio-capillary disease.

There is thus considerable excuse for the belief that albuminuric retinitis—or albuminuric neuro-retinitis—is but another expression of a toxic process of pre-renal origin, other expressions of which may be (not necessarily are) changes in the arteries and capillaries and kidneys and constant or occasional albuminuria.

As to the nature of the pre-renal toxic agent, it is a tempting hypothesis to consider that terminal infections are the cause of the albuminuric retinitis and of the accompaniment (excepting Case 37) of albuminuria in each of these eleven cases, for a terminal infection was present in every one of them. Such an origin of the cause for albuminuria and albuminuric retinitis is, however, not supported sufficiently, for Case 1 showed albuminuria, but no albuminuric retinitis, and at the post-mortem examination there was no terminal infection (the tubular degeneration met with in this case must have been due to some pre-renal undefined toxin other than infection). Similarly in Cases 30, 48 and 50 albumen was present, albuminuric retinitis absent; capsulitis and associated tubular disease were present, but no tubular degeneration and no terminal infection: in these cases, too, an unknown toxic agent of pre-renal origin must have been operative, other than infection.

To continue with the analysis made in Table III., reference to Mr. Lawrence's scheme of the causes of atrophy of the glomeruli and tubules shows that the Small

White Granular Kidney is really a parenchymatous disease of the organ, in that it is due to capsulitis and atrophy of the glomeruli, followed by atrophy of the tubules; that the well-known Red Granular Kidney is the result of the necrotic atrophy of the glomerular tuft due to occlusive disease (endarteritis or thrombosis) of the afferent vessels of the tufts, which is followed by atrophy of the tubules, and that the Secondary White Kidney, or Contracted White Kidney, is the result of destruction of the glomeruli and tubules by a degenerative change of the cells of these structures independent of vascular occlusion. It is clear that such classification cannot depend upon naked-eye examination, and as he has provided such an exhaustive inquiry into the minute anatomy of the kidneys in this series, it is infinitely preferable to discard all naked-eye descriptions and to study these kidneys on a purely histological basis. Table III. shows an analysis of his findings. The interpretation of these analyses is best shown by taking an example—say Case 8—50 per cent. of the glomeruli appeared to be normal: the cause of the abnormality (atrophy) of the remaining 50 per cent. was dual—part were atrophied from capsulitis and part from occlusive vascular (arterio-capillary) disease: a corresponding number of tubules (probably 50 per cent.) were also atrophied as a result of the capsular atrophy: only a few tubules were normal: those tubules which were not atrophied but which were not normal showed degeneration, *e.g.* cloudy swelling and granular change.

Case 1 showed that almost all the glomeruli were atrophied from arterio-capillary disease: many tubules were atrophied, partly as the result of the disorder of the glomeruli and partly as a result of the direct effect of the arterio-capillary disease upon them: most of the tubules which had escaped atrophy from either of these causes showed degeneration in that few tubules were left normal in appearance. Case 48 shows that in the left kidney 10 per cent. of the glomeruli were atrophied, in part from capsulitis and possibly in part from the mechanical agency which caused marked hydronephrosis of the right kidney. Many tubules were atrophied, partly as a result of the capsulitis, but mainly as a result of the causes of the right hydronephrosis: the glomeruli and tubules of the right kidney suffered very markedly from the effects of carcinoma of the bladder, which produced hydronephrosis of the corresponding kidney.

The microscopic examination of the kidneys makes it possible to group them in accordance with the changes met with in the glomeruli and tubules.

Group 1.—Capsulitis and resultant capsulitic and tubular atrophy—Cases 30, 33, 35, 48 (left) and 50.

,, 2.—The same changes as Group 1, + degeneration of the tubular epithelium—Cases 5, 9, 20, 22, 29, 31, 32 (left), 37, 40, 41, 42, 43 and 45.

,, 3.—The same changes as Group 2, + atrophy of tubular epithelium from vascular disease—Cases 8 and 49.

,, 4.—The same as Group 1, + atrophy of tubular epithelium from vascular disease—Cases 4, 7, 10 and 14.

,, 5.—Atrophy of glomerular tuft from hyaline capillary disease and resultant atrophy of tubules, + atrophy of tubules from arterial disease—Case 3.

,, 6.—Atrophy of glomeruli and tubules from vascular disease, + degeneration of the tubules—Case 1.

An opportunity is now given of estimating quantitatively (at best only roughly) and qualitatively the value of the total renal substance represented in the kidneys in each case, and at the same time showing the relationship of the microscopic efficiency of the kidneys with the clinical estimate of uræmia.

Case 1, in whom there was no terminal infection which could complicate the clinical picture and yet showed an almost complete loss of glomeruli and tubules from vascular occlusion (to which is added some degeneration of the few unatrophied tubules), died "uræmic." The clinical symptoms are such as may therefore be considered as due purely to death of the kidney tissues from ischæmia—hyperpiesis, loss of consciousness, slight fits, anuria for at least three days, vomiting, dyspnœa, weakness, hæmatemesis, epistaxis, puffiness of the lids, thirst, nycturia, albuminuria, hyaline, epithelial and granular casts: no dropsy, no neuritis or retinitis, no retinal hæmorrhage: no petechiæ: heart-weight, 13 oz.: Red Granular Kidneys, each weighing 2½ oz.: although slight fever had been found during life, no post-mortem evidence of terminal infection. The extraordinary feature of this case is that she had been ill on and off for three or four years before death, and that at the moment of death almost all the glomeruli and tubules were *atrophied* (not merely degenerated). Life seemed possible until the merest vestige of unatrophied parenchyma was left!

Death occurred because almost the last vestige of healthy renal substance had gone—the usual constituents of the urine could no longer be excreted. This sort of evidence has been held to constitute the proof that "uræmia" is due to the inability of the kidneys to extrude the waste products of metabolism. Experiments have failed to show which are the metabolites responsible for the "uræmia," so that it is not to be wondered at that other sources of poisoning have been looked for. The problem has been attacked from the endocrine point of view in the hopes of showing that really what led to the poisoning of the patient was the loss of some substance naturally secreted into the body by the kidney whilst normal: when the kidney, as in this case, no longer existed such endocrine secretion was absent, and hence the poisoning, as if "uræmia" was due not to retention of metabolites, but to the absence of substances derived from healthy renal substance.

But when other cases such as 30, 33, 35, 48 (left) and 50 are examined in the light of endocrine deficiency, *i.e.* cases in which capsulitis has produced atrophy of the glomeruli and associated tubules, it is found that in Case 33 with the destruction of 60 per cent. of the corpuscles and associated tubules death was not due to "uræmia" but to terminal infection: in Case 50, with 50 per cent. of glomerulo-tubular atrophy death was due to cerebral hæmorrhage, and not to "uræmia"; and that in Case 30 with 24 per cent. of glomerulo-tubular atrophy "uræmia" was not the cause of death: moreover, that in cases in which only 10 per cent. of glomerulo-tubular atrophy was present, the remaining elements being normal and free from degenerative changes of any kind, "uræmia" *was* the cause of death: and further, in Case 48, in whom, despite the hydronephrotic condition of the right kidney, the left kidney hypertrophied to 10 oz., showing only 10 per

cent. of glomerulo-tubular atrophy, the remaining elements being quite normal, "uræmia" was *again* the cause of death, there can be no hesitation in saying that "uræmia" is not due to either the want of sufficient parenchyma to excrete the metabolites of the body, or to the want of secretion of endocrinic substance. The causes for the "uræmia" must be sought elsewhere, and it is clear that there is but one other source for the "uræmia," namely, hypothetical toxins circulating in the blood, which produce their effects quite regardless of whether there is no excretory or secretory parenchyma of the kidney (Case 1) or 90 per cent. (Case 35). The cause of "uræmia" would appear not to be due to retention of metabolites or to want of endocrine bodies, but to the presence of poisons so far undetermined in character and resident in the blood. No doubt bacterial infection (pneumonia) can add special features, as in Case 48, but in Cases 1 and 48 terminal infection could not be recognised naked-eye, although in Case 1 there was evidence during life of fever.

The second group above referred to gives an opportunity for examining the effect not only of glomerulo-tubular atrophy from capsulitis, but of the added element of degenerative change in the tubules presumably originating from some toxic agent present in the blood and leading to such change.

"Uræmia" is given as a cause of death in only two cases, namely, Cases 5 and 22: in Case 22 there was 70 per cent. of glomerulo-tubular atrophy, and the remaining capsules and tubules were capable of functioning, though the latter showed degenerative changes. The efficiency of the kidneys in this case came to as low a level almost as that in Case 1, and similar "uræmic" symptoms developed, including suppression of urine: the presence of pneumonia, however, confused the picture, and may have accounted for the tubular degeneration and for the death. In Case 5, however, there was 98 per cent. of normal capsules, giving an associated 2 per cent. of atrophied tubules, and a very large number of degenerated tubules which possibly owed their change to erysipelas. Despite 98 per cent. of normal capsules, ascites and dropsy were marked features. Possibly the toxic process underlying the cirrhosis of the liver was responsible for these phenomena. How much infection present on admission, as shown by fever and as shown by erysipelas towards the end, was responsible for some of the toxic features it is impossible to say, but the "uræmia" may fairly be considered to have been due, in view of what has already been said, to some pre-renal poison in the blood.

ANALYSIS OF THE MICROSCOPIC CHANGES MET WITH IN TWENTY-ONE OF THE FORTY-SEVEN KIDNEYS WHICH WERE *NOT* INJECTED WITH PRESERVATIVE FLUID SHORTLY AFTER DEATH, *i.e.* BEFORE POST-MORTEM AUTOLYTIC CHANGES COULD HAVE BEGUN.

The cases under consideration are Nos. 2, 6, 11, 12, 13, 15, 16, 17, 19, 23, 24, 25, 26, 28, 34, 36, 38, 39, 44, 46 and 47.

It is not desirable to carry a close analysis into the domain of these remaining twenty-one cases in whom it was impossible for various reasons to inject the kidneys

TABLE V.—SHOWING DETAILS OF THE KIDNEY CHANGE IN TWENTY-ONE CASES, THE KIDNEYS NOT BEING INJECTED BEFORE AUTOLYSIS COULD HAVE OCCURRED

No. of Case.	Clinical Evidence of Disorder of Kidneys.					Microscopic Evidence of Functional Capacity of		Cause of Parenchymatous Atrophy.		Recent or Terminal Tubular Degeneration.	Clinical Cause of Death.	Terminal Infection (found at P.M.).
	Non-elimination or Suppression of Urine.	Albuminuria. Constant	Albuminuria. Occasional.	Retinal Change.	Dropsy or Effusion.	Glomeruli.	Tubules.	Ischæmic or Vascular.	Toxic Non-vascular.			
2	0	Almost +		+ (A. R.)	+φ	90 per cent.	Many	0	+	+	? Cardiac failure	0
5	0	Almost +		+ (A. R.)	0	Most	Most	0	+	+	Apoplexy (and uræmia)	0
11	0		+	0	0	70 per cent.	Many	+	Slight	+	Cardiac failure	+
12	0		+	0	+	85 ,,	,,	0	+	+	Carcinoma of stomach	0
13	0	0	0	0	+	93 ,,	,,	0	+	+	Carcinoma of œsophagus	+
15	? +	+		+ (A. R.)	+	A. 70 ,, B. 50 ,,	,, ! Few	A. + B. +	Slight	A. + B. +	Uræmia	+
16	0		+	No report	+φ	79 ,,	Many	Slight	+	0	Terminal infection	+
17	0	+		+ (A. R.)	+	? 80 ,,	Moderate number	+	+	+	Uræmia, ? pneumonia	+ (ascending nephritis)
19	0	+		0	0	10 ,,	Few	+	0	0	Terminal infection	+
23	0		+	No report	0	78 ,,	Many	+	Slight	+	Cardiac failure	+
24	0		+	0	+φ	96 ,,	Most	0	,,	+	Uræmia	0 (? cellulitis)
25	0	+		+ (A. R.)	+	70 ,,	Many	+	+	+	Terminal infection	+
26	0		+	No report	+ ? φ	about 100 ,,	Most	0	+	+	Pulmonary tuberculosis	?
28	0		+	,,	+	A. about 40 ,, B. more than 40 per cent.	Few Many	+	+	+	Terminal infection	+
34	0		+	+ (A. R.)	0	96 per cent.	,,	0	Slight	+	Meningeal hæmorrhage	+
36	0		+	0	+φ	68 ,,	68 per cent.	Slight	+	+	Cardiac failure	0
38	0		+	+ (A. R.)	0	63 ,,	Most	+	Some	0	Uræmia	0
39	0	+		+ (A. R.)	+	R. 30 ,, L. Few	,, Few	+ +	Slight	0 0	Uræmia	+
44	-		+	No report	+	64 ,,	Many	Slight	+	+	Cardiac failure	+ (Decubitus)
46	+	+		0	+	95 ,,	Most	0	Slight	+	? Uræmia ? Cardiac failure	0
	-	+		No report	+	+ ,,	,,	+	+	+	Uræmia	+

φ = Complicated by valvular disease of heart.

A. R. = Albuminuric retinitis.

with preservative fluid shortly after death, for although the propositions put forward in the last pages would receive support from the discussion, the evidence is tainted at its source by reason of the possibility that the kidneys were not kept in close approximation to their condition during life. A table of the analysis is given so that the reader may, if he desires, test the conclusions arrived at. (Table V.)

It will be seen that the injected kidneys numbered twenty-six and the uninjected twenty-one cases : sixteen of the former group, *i.e.* 60 per cent., showed degenerative changes in the tubules, and it may be presumed that these were not of an autolytic nature : seventeen of the second group, *i.e.* 80 per cent., showed degenerative changes in the tubules. As this latter group of kidneys may therefore have undergone autolytic changes, the increased percentage may be explained on that ground. It is, however, possible that they represent toxic effects, independent of autolytic change. Thus an element of doubt hangs over any analysis of the changes met with in the second group. Presumably autolytic change accounts to some extent for the greater percentage of tubular degeneration in the second group, because terminal infection, which may have been responsible for the tubular degeneration noted, was present in 76 per cent. of the first group and in only 60 per cent. of the second one.

Attention, however, may be drawn to certain of the cases. Case 24 was one of extraordinary interest. As the charts show, she was under observation for a considerable time, and hyperpiesis was present to a marked degree during the great part of her stay in the hospital, and eventually a few weeks before death it disappeared. Her symptoms gave rise to difficulties in diagnosis. On admission the symptoms and signs (except the hyperpiesis) and the history gave excellent reasons for thinking that her disorder was entirely due to mitral disease engendered by rheumatic fever, failure of the cardiac muscle and the development of œdema of the lung—familiar manifestations in such cases. In March and in May she developed paroxysms of tachypnœa, so long known as " cardiac asthma," but which have been shown to be probably closely related to reduction of the alkalinity of the blood. Drainage of the legs was carried out for the relief of the dropsy in July, and from then onwards the hyperpiesis gave place to normal and subnormal pressure readings—a result which, alas! too often has ultimately been shown to be due to ensuing cellulitis of the tissues of the legs, bacterial toxins having caused the fall of the blood-pressure. A striking feature now made its appearance, for on July 27 she developed fits of a " uræmic nature," and these fits were repeated till her death on July 31 : albumen had been found on several occasions, but on a less number of occasions was absent. So striking were the fits that the clinician in charge had no hesitation in describing them as " uræmic," and that they were due to granular kidney, an opinion in which the writer entirely concurred, for he had been responsible for the observations on the blood-pressure, and had felt largely, in obedience to time-honoured teaching, that there could be no doubt that the kidneys would have presented the features so familiar as those of granular kidney.

The surprise revealed by the post-mortem was most complete. Naked-eye examination showed kidneys weighing 6 and 7 oz., with smooth surfaces, untoughened substance but marked congestion, dependent, as in the case of the liver, upon mitral stenosis and cardiac muscular disease. Microscopically, however, some fibrosis of the kidneys was found around the vessels of the boundary zone, producing no effect on the cortex : 96 per cent. of the glomeruli were normal, 4 per cent. only being damaged by capsulitis. Only small scattered areas of tubular atrophy were found, probably consecutive to the capsulitis, but many unatrophied tubules were found which showed cloudy epithelium, and in some tubules there was much desquamation : no doubt these recent changes were due in part to congestion and in part to the effects of cellulitis following drainage of the legs. The interlobular arteries showed only slight sclerosis !

What was the origin of the suggestive " uræmic fits " ? There can be but one conclusion, namely, that at any rate in the light of the microscopic findings they could not be held to be indicative of serious widespread damage to the kidneys.

It will be remembered that they had never occurred in this case up to the moment of the drainage of the legs, and the writer considers that it is possible that the operative measure of drainage of the legs, by allowing infection, or increasing infection, led to the development of the fits. Another effect, as we have already seen, of the same operation, was that hyperpiesis soon gave place to a condition of low blood-pressure. The view thus enunciated may cause the reader to feel that too great a burden has been laid upon the back of the principle of infection, and that the production of convulsive seizures has been, and always will remain, a characteristic phenomenon connected with kidney disease. But, after all, a great novelty has not been put before the reader : uræmic fits are certainly due to the effect of irritant substances, or agencies, acting upon susceptible portions of the brain : it used to be thought that the substances causing these fits were those metabolites unable to escape through the kidneys : all that this case forces us to do is to admit that though irritating bodies were present in the blood-stream and produced the fits, they were present there in sufficient amount, not because they had not been able to escape, owing to the kidneys being diseased, for they were healthy, but owing to the fact that they were being produced in pre-renal sites, and gained access to nervous tissue which could react and produce fits.

In only two cases (Nos. 15 and 46) was suppression of urine said to have occurred. Liberty has been taken, however, with the notes of Case 15, for in these it is stated that retention of urine occurred and not suppression : the kidneys in this case were small, weighing 2 and 3 oz. : they were also " scarred " kidneys : the scarred areas showed almost complete atrophy of the Malpighian corpuscles, and the unscarred, atrophy of only 30 per cent. of their elements. Chronic parenchymatous nephritis was found by Mr. Lawrence in all the tubules which had not undergone atrophy. It is therefore quite possible for anuric symptoms to have contributed largely to the death which was said to have been due to " uræmia " : again it is impossible to say how much or little the terminal infec-

tion which was present in the form of pneumonia, empyema and pericarditis was responsible for the symptoms during life. The anuria is difficult to explain, seeing that in the unscarred parts of the kidney so many corpuscles were not atrophied. There is room for the views of those who hold that "uræmic" symptoms are due to the failure of the epithelium of the tubules to excrete metabolites, for those tubules which had escaped atrophy showed widespread parenchymatous nephritis of a chronic character. There is, however, as good reason to believe that the widespread parenchymatous degeneration and the "uræmic" symptoms were due to some general cause existing in the blood-stream. Case 46, as already pointed out, would be considered by some observers to have died "uræmic," but there can be little doubt that cardiac failure was a more expressive term to use for the cause of death, and that the scantiness of the urine towards the end of life was due to that cause and not to failure in the efficiency of the kidneys, which weighed 10 oz. each and microscopically showed atrophy of only 5 per cent. of the Malpighian corpuscles and associated tubules: the degeneration found in the bulk of the tubules could not have been due to terminal infection, as this was absent.

It would thus be seen that of the forty-seven cases studied only two cases, Nos. 1 and 22, gave good opportunity for the close study of the microscopic analysis of the kidney and the relationship of the changes found to "uræmia." Suppression of urine (anuria) was present in both cases: the symptoms met with at the bedside were those of what is spoken of as "uræmia." Case 1 alone gave the complete picture of total kidney degeneration, so far as the parenchyma was concerned, and there was no terminal infection. Case 22 was a complicated one, for pneumonia played its part in the cause of death. Moreover, there was still 30 per cent. of normal glomeruli and a fairly large number of tubules which, though showing degenerated epithelium, were capable of functioning. Case 1 stands out as the only one in whom "uræmia" was present during life uncomplicated by terminal infection and accompanied by complete annihilation of the kidney parenchyma. That the patient could have lived up to the final moment of the destruction of the last few corpuscles and tubules is remarkable and gives good reason for the belief that there was a pre-renal toxic cause, both for the so-called "uræmia" and destruction of the kidneys, and also for the constant presence of albumen in the urine.

Albumen was found constantly, or almost constantly, in Cases 2, 6, 15, 17, 19, 25, 38 (at end), 39, 46 and 47. It was only occasionally present in Cases 11, 12, 16, 23, 24, 26, 28, 34, 36, 38 (at beginning) and 44. Albumen was absent in Case 13.

The circulating toxins in these cases may be manifold; but it may be that they are very few indeed, and that the extremely variable results of their presence in the blood-stream depends not only upon the extremely variable functions of the tissues and organs bathed by such blood, but upon the variability of the susceptibility of such tissues and organs to these poisons at different hours in the day, or days in the week, in the same person, or upon different degrees of susceptibility of the same type of tissue or organ in different individuals.

Is Hyperpiesia a Disease?—This is a question which should at this stage be

answered. The forty-seven cases have been studied not only to endeavour to establish what is the relationship of Hyperpiesia to kidney disease, but also to glean information on the features of Hyperpiesia and their mode of development. Sir Clifford Allbutt has effectively answered the above question in his two notable volumes on Diseases of the Arteries. He has come to the conclusion that Hyperpiesia is "a malady in which at or towards middle life blood-pressure rises excessively, a malady having a course of its own and deserving the name of a disease" (vol. i. p. 10). It "may appear at any age; it is no infrequent contingent disorder in elderly people, when, if detected in good time, it is usually curable; if not, however transient, it is a serious menace to decadent structures" (*ibid.* p. 170). "A certain disease—that is to say, a fairly uniform recurrent series and correlation of symptoms positive and negative—is to be recognised and delineated, which, although marked from the outset by a rise of arterial pressures, does not follow the clinical course of Bright's disease in any of its modes, but manifests itself by symptoms which I have described elsewhere in this book" (*ibid.* p. 344). "Of Hyperpiesia I have never offered an explanation, or nothing more than conjecture; I have been content to distinguish it as a clinical series from the recognised forms of Bright's disease" (*ibid.* p. 345).

It might be thought unfair to Sir Clifford's conception to broaden the base of the pyramid and include in the disease cases, for example, who never recover, who are at first found to be abnormal by the accidental discovery alone of hyperpiesis, and who finally pass through the stages in which it is impossible to say that they have, or have not, grave renal disease; indeed, some of them may die as if they had been cases of granular kidney. On the other hand, such cases may never present any of the similitudes of kidney disease, but may die of the accident of cerebral hæmorrhage, or of the more numerous accidents of terminal infection. We are bound to hold a very comprehensive conception of the condition we are discussing; for I fear that if we said a patient at one stage of his life was suffering from a disease—Hyperpiesia—and because at a subsequent date the picture changed owing to the addition of other manifestations we called it something else, endless confusion would occur. If ever Hyperpiesia is found of a persistent, and even of a permanent, character, I would make this the distinguishing thread of the fabric, whatever other additions or subtractions may have occurred. Hence it is quite possible to find a case of Hyperpiesia combined with various forms of heart disease, lung disease, kidney disease, Graves' disease, etc. The great question now is, has anyone ever met with a case of fatal Hyperpiesia in its simplest form—that is to say, has any patient been found to die as a direct result of those clinical departures from the normal met with in Hyperpiesia? The only symptoms that a person has are those that are referable to the hyperpiesis itself, or to the cardiac hypertrophy, or to the mesarterial hypertrophy which eventually results from the maintained and long-continued hyperpiesis. In this series of forty-seven cases very few indeed encourage the belief that they may have died from Hyperpiesia in its simplest form. If a patient suffered from symptoms of Hyperpiesia, but died of cerebral hæmorrhage, the post-mortem examination provided ample opportunity for

studying the heart, kidneys and blood vessels at a particular stage of development which had been reached by the disorder when the cerebral vessel ruptured, but it cannot be said that the post-mortem examination gave an opportunity of studying the body of a patient whose death was directly due to Hyperpiesia. The same remarks apply to the cases in whom Hyperpiesia existed concurrently with some other disease, and the concurrent disease caused the death of the patient, for example, carcinoma of some part of the body. But when we turn to those cases whose deaths appear to have been brought about by some terminal infection, such as pericarditis, pleurisy, pneumonia, cellulitis, etc., it is difficult to say that death is, or is not, due directly to the Hyperpiesia, because it does appear, from the frequency with which terminal infection occurs in these cases, that possibly the tendency to develop terminal infection is a feature of Hyperpiesia. It is impossible to say it is, or is not, until figures are collected to show how frequently terminal infections are met with in other disorders which during life presented such a special fatal feature, say as primary anæmia, etc. etc. Until this question is accurately settled it would be unwise to assume that terminal infection is a special feature of Hyperpiesia.

But two cases now to be referred to afford some opportunity for studying the post-mortem findings in subjects of Hyperpiesia who appeared to die merely of the Hyperpiesia and attendant symptoms : and these symptoms, so far as could be ascertained, were not expressive of terminal infection or other complicating diseases, such as cancer, heart disease, kidney disease, etc.

Case 45.—During life this patient had suffered from palpitation, shortness of breath, pain over the heart, cough, and was found on examination to have a large heart presenting the usual signs of hypertrophy. The urine was examined four times, and on three occasions albumen was found ; the amount of urine amounted to 900 to 1200 c.c. in the twenty-four hours ; the brachial artery was tortuous and there was dropsy ; the pulse was irregular. Without any warning the patient died suddenly in bed. The heart was found to weigh $17\frac{1}{2}$ oz., and was hypertrophied ; there was slight atheroma of the aortic and mitral valves ; œdema was present in the legs, as well as bilateral pleural effusion ; the liver presented a "nutmeg" appearance. The kidneys weighed $5\frac{1}{2}$ and 6 oz. respectively ; their surfaces were finely granular, and a few scattered cysts were present. The pathologist returned as the post-mortem diagnosis, "chronic interstitial nephritis." The microscopical examination showed that 97 per cent. of the glomeruli were either normal or if slightly altered were capable of functioning. There were only small areas of tubular atrophy and fibrosis. Many of the tubules showed epithelium which was swollen and granular ; there was no extensive disease of the renal blood-vessels. There can be little doubt that the diagnosis "chronic interstitial nephritis" hardly covered the clinical features of the case, because the irregularity of the pulse is an indication of disturbance of the heart's rhythm by agencies affecting its nervous control, or its conducting mechanism, so that to some observers the actual cause of death in this case would be considered to be heart failure ; but then, again, it is reasonable to advance the view that the heart

failure would not have occurred had not some poisonous agent arrived upon the scene and disturbed the heart's action, and the problem is rather not what particular naked-eye or microscopic change was present in any organ which might excite the observer's interest, but what poisonous body or bodies were responsible for the fact that dyspnœa, cough, dropsy, albuminuria, irregular pulse and death should occur in an apparently uninfected subject with slightly altered kidneys and a large, hypertrophied heart? It is idle to speculate whether the poisons circulating in the blood were many or few, whether one was responsible for the irregular pulse and a different one for all the other symptoms present in this case; but at least it may be said that the poisons responsible for the majority of the symptoms met with in Hyperpiesia do not provoke irregularity of the pulse, and that therefore in this particular case death was due not to the poisons of Hyperpiesia, but to some other poison, the special affinity of which was, say, the conducting fibres of the heart. It is, however, quite possible that the poisons of Hyperpiesia are capable of producing irregularity of the heart when its conducting fibres have been disturbed in function by some previous infection. In other words, neither cause would be sufficient in itself, though both acting together were capable of bringing about the death of the individual. Thus it looks as if in the present imperfection of our knowledge it were mere quibbling to assign death to its proper cause in this case, seeing that the only causes admitted are hypothetical ones. Unsatisfactory as this state of affairs may be, it is no more so than to rest satisfied with the view that the patient succumbed to chronic interstitial nephritis.

Case 46.—This case appeared to be suffering from cardiac disease: murmurs were even heard indicating double mitral disease: ascites and occasional dropsy of the feet were observed; there was constant albuminuria; casts were seen occasionally, and hæmaturia had been noticed once or twice; the chart was characteristic of Hyperpiesia; the liver was enlarged; the cardiac area was increased to the right and left; the aortic second sound was accentuated. The patient was of healthy complexion and was a well-nourished man: dyspnœa was a very marked feature, and numerous sonorous and sibilant rhonchi were heard over both lungs; the retinæ were free from changes. Irregularity of the pulse developed, which, however, was shown to be due merely to functional disturbance of the conducting fibres of the heart. In the course of time he recovered sufficiently to be able to leave the hospital and go home; but eventually he returned, and death took place quietly, but with dyspnœa unaccompanied by any signs in the lungs. In view of the physical signs indicating valvular disease, many clinicians would naturally have concluded that the patient died of cardiac failure, but the characteristic hyperpiesic chart and albuminuria, hæmaturia and the presence of casts, would give others reason for believing that death had occurred from the respiratory form of "uræmia."

At the post-mortem no terminal infection was found; the heart was hypertrophied and weighed 39 oz.; the valves were quite normal; each kidney weighed 10 oz., was large, had a smooth surface, and was a little tough. Microscopically the kidneys showed trifling glomerulo-tubular atrophy (5 per cent.), a few narrow

tracts of tubular atrophy and fibrosis and practically normal blood vessels ; the bulk of the remaining tubules showed swelling and granularity. Thus the post-mortem examination gives considerable support to the view that death had occurred from Hyperpiesia. If the condition of the tubular epithelium of the kidney is raised as an objection to such a diagnosis, and it is insisted that really after all the case was fatal in a "uræmic" sense, and that the kidney had failed in its proper function, then it may be pointed out that mere swelling and granularity of the tubular epithelium is no bar to the proper functioning of the cells, because similar changes have been met with in other cases where the kidneys appeared to be functioning in an almost normal way ; so that it seems more reasonable to conclude that this patient was suffering from a pre-renal toxæmia which led to functional disturbance of the heart, to an œdematous condition of the lungs, and possibly to the slight granular disorder of the kidney epithelium, and finally death was brought about not from organic disease of the heart, but from a cardio-pulmonary failure resulting from the toxæmia. It will be seen that the blood gave a positive Wassermann reaction.

In offering these two cases as examples of the fatal results of Hyperpiesia the same sort of difficulties are met with when we ask ourselves at the post-mortem table what is the actual cause of death of any particular case ; for example, cases which have succumbed to valvular disease of the heart may reveal perfectly healthy heart muscle to the naked eye, and valves free from recent endocarditis ; degenerative changes may be found in the cardiac muscle by the microscope, but it would be difficult to say whether such degenerative changes were the result of the toxæmia resulting from the infection which appears to be present in so many cases of chronic valvular disease, or whether they were caused by toxæmia originating from the patch of pneumonia at one or other base. The probabilities are, we should confess to ourselves, that the patient had died, as so many cases of valvular disease do die, from some infection, and that the patient's death was actually brought about by the accumulation of the blood in the capillary bed, and yet we should not hesitate to give the cause of death as being cardiac failure. In the same way with regard to these two cases probably they, too, eventually would be claimed to have died from cardiac failure, the one suddenly and the other more gradually, both having shown irregular pulse at some time or another, and both showing evidence during life of symptoms that were very suggestive of cardiac failure. The picture, however, at the post-mortem of large hypertrophied hearts met with in both cases reminds one of Sir Clifford Allbutt's apt description that they were both "defeated" hearts, but not diseased ones, and that death really had come about by the stagnation of the blood in the capillary bed. Reasons will be given later on for the explanation of this cause of the cardiac failure in these two cases, and efforts be made to show how it is possible for cardiac failure, or rather cardiac "defeat," to become a salient feature of death from Hyperpiesia.

SECTION III

THE ORIGINS OF HYPERPIESIS AND OF "IDIOPATHIC" CARDIAC HYPERTROPHY

HYPERPIESIS is the expression of the fact that at each systole of the heart the blood within the arterial system is subjected to an increased propulsive force. The normal propulsive force shows itself by a systolic advance of the blood along the arteries, but part of the force is stored as a reserve of energy by expanding the arterial walls, which on recoil communicate to the blood a further propulsive movement onwards at a time when the cardiac systole has given place to diastole: thus in each cardiac cycle the blood experiences two forward movements instead of one. In hyperpiesis the force of these two movements is increased, and it is observed that not only systolic, but diastolic blood-pressure in every artery is raised. How is this increase of blood-pressure brought about? The days have gone by for invoking a *deus* or a *diabolus ex machina* in the form of a physiological peculiarity: there must be a demonstrable cause for such an extraordinary effect. It is quite a reasonable proposition to offer, that extra work on the part of the heart during muscular activity would increase the blood-pressure, but it is another matter to propose that this enhanced blood-pressure would continue to exist when the necessity for increased muscular activity has passed off: reserves of food supply, etc., must be summoned to replace the chemical waste in the cardiac muscle, and although this must, and does, take place whilst extra work is carried on for a longer or shorter period, according to the endurance of the will of that individual and the power of the individual cardiac muscle, a time will at last come when rest is imperative. Blood-pressure observations after severe muscular activity show a fall to normal or to subnormal. Is the source of increased energy on the part of the musculature of the heart and blood vessels to be found in any centric discharge of nervous energy controlled not by the will but by subconscious automatic and reflex centres? No doubt this is possible, for it is a common experience that the excitement of a medical examination is enough even in the most composed patients to give a false impression of what is the degree of blood-pressure. A night's rest will be frequently found capable of changing a reading of 160 mm. for the systolic blood-pressure to one of a lower degree, and it is frequently found that individuals after a continuous rest in bed for a few days will show on each day a steady fall of pressure from a considerable height to the normal; but such forms of raised blood-pressure as these do not appear to be associated

with those permanent changes in the heart and blood vessels which are familiar when the blood-pressure has been raised for weeks, months or years, as in Hyperpiesia, a condition which is the special object for consideration in this study. Great increase of the intracranial pressure such as is produced by a sudden intracerebral hæmorrhage is well known to cause a persistent (so long as the intracranial pressure operates) and indeed very high degree of hyperpiesis, and was operative in part in some of the cases of this study: they were the exceptions, however, and the large remainder revealed no such coarse disturbance of the intracranial tension. Can occlusive, *i.e.* obliterative, disease of the arteries and arterioles in any extensive or restricted area cause a rise of pressure of a permanent or persistent character? The results of ligature of the aorta at the level of the diaphragm, and of the large vessels of an amputated limb or of a kidney or of the spleen, do not encourage this view. But could a gradually increasing and final closure of all the smaller arteries of the body by occlusive disease not succeed when more limited and sudden ligature has failed? The facts that hyperpiesis has been shown to occur in the forty-seven cases already described, and that histological examination of some of the kidneys (in which organs numerous arterioles are on view closely packed together) shows that occlusive disease of these arterioles is absent, give a negative answer to such speculation. Further objection is found for this explanation by the study of the blood-pressure charts in purely hyperpiesic subjects, *i.e.* in persons who beyond having permanent hyperpiesis show no signs or symptoms that hyperpiesis has become complicated by the common terminal infections. It will be seen that the pressure curves are not maintained at a stated level—they vary sometimes by rises and falls within extremely wide limits. If the occlusive disease of the arteries can pass off within a few days and return again, these rises and falls could be explained. But it is inconceivable that such arterial disease could pass off and return again so quickly. It may, however, be argued that in hyperpiesic subjects the vaso-motor control of the arteries and (or) the functional power of the heart on these occasions are temporarily disturbed, a fall of pressure being the result of a temporary relaxation of the central or peripheral vaso-motor control of the arteries, or by a temporary weakening of the cardiac power, or by the occurrence of both, and a rise of pressure being the result of a temporary central or peripheral increase of the arterial tonns, or by a temporary increase of the cardiac power, or by the occurrence of both. But then it must be admitted that there is no proof that any of these changes can be brought about except as a result of the effect of chemical influence upon the neuro-muscular junctions, or upon the heart muscle. Spontaneous reflex contraction or relaxation of the arterioles lasting for several days is unknown to physiology, nor is there any evidence that such relaxation or contraction of the arterial tissues could be brought about by spontaneous changes in the vaso-motor systems.

It is a more reasonable proposition to advance, that at the neuro-muscular junction agencies can operate which are chemical or physical or chemico-physical, and that they are bodies which may be carried by the blood. Experimentally

it is established that the toxins of bacterial origin operate at such sites, and that they are almost universally depressor in action—they almost all act, when they do act, by lowering the blood-pressure. Are there bodies which could act at this site which are pressor in function ? We are aware of a very few, but their action and importance is established. If the blood-stream supplying the heart and blood vessels is charged with pressor agents capable of acting at the neuro-muscular junction, then there is a ready explanation for hyperpiesis, and if the strength of solution in the blood of these bodies varies, there is a ready explanation for the variations in the reading of a hyperpiesic chart.

If such an assumption appears too fanciful, there are others which can vie with it, and eclipse it in imaginative brilliance. One limited district of the systemic circulation suffers from occlusive arterial disease : the remainder of the circulation, including the heart, "senses" the localised obstruction and proceeds by increased cardiac action and by increased vaso-motor constriction in the healthy parts to continue to charge the districts suffering from anæmia, with the due amount of blood ! The imagination is asked to invoke a special power on the part of the circulation to locate the threatened area and to call up adequate increased force to save it ! As a further example of far-fetched speculation the vascular system, including the heart, has the special power of divining that there are faulty substances in the circulation which once gaining access to tissues and organs will lead to their destruction : they must be prevented from gaining such access by closing the arteries through the vaso-motor mechanism, and as a result the heart works with more power and the blood-pressure rises ! Or, again, in such circumstances, the heart works harder in order to rid the system of the peccant agents circulating in the vessels, by sending all the blood of the body at increased rates through the renal system for depurative purposes, the kidneys either resisting, suffering from, or being destroyed by the poisons during the process !

With so many hypotheses to choose from there can be no harm in choosing one which seems least objectionable and most in conformity with knowledge, and which opens the way for investigation, clinical, pathological and experimental. For this reason the conception followed in the whole of this study has been that possibly the problems connected with the subject of hyperpiesis will find a solution in the establishment of a toxic theory—no new project, but one hallowed by the work of Bright himself and presenting a wealth of opportunity for further investigations. There is in recent years no lack of encouragement from physicians, ophthalmic surgeons, chemists, pathologists and others, for they are ready to invoke a toxic cause, or causes, for the production of Hyperpiesia and its constantly associated cardiac hypertrophy and less constant vascular alteration, and for the other frequent occurrences of albuminuria, kidney disfiguration, and the numerous disordered functions which are so familiar. It has still to be settled whether there is only one toxic agent which can produce hyperpiesis, or more than one, and also the origin of such agencies : it is still undetermined whether the cardiac hypertrophy is a direct or indirect effect of the operation of hyperpiesic agencies, or why it is that so many of the cases show albuminuric neuro-retinitis, obvious or

less obvious kidney disease, dropsy, dyspnœa, convulsions, coma, paralysis, general or local septicæmia, etc.

"IDIOPATHIC" CARDIAC HYPERTROPHY.—This subject is one which has caused much debate. At the present moment there is no knowledge of the mechanism whereby any muscle, let alone the cardiac muscle, hypertrophies. When a muscle contracts, heat and energy are liberated, waste products result; these "ashes" are removed: fresh muscle food is supplied to renew the muscular energy; ordinarily just so much renewal occurs as to replace the lost muscle substance, but what determines there shall be a balance and not a minus or plus renewal? Until the answer is given it is fruitless to try and answer the question how is it brought about that the renewal is *greater* than the original loss, and that hypertrophy takes the place of the *restitutio in integrum*? How needful is an adequate answer is shown by the confession of physiologists that there is none at the present day. It is not known why the voluntary musculature can be raised to a certain pitch of healthy increase by training, but can go no further. It is not known how the heart can treble its weight by what appears to be an increase of the size of its individual fibres. Nor must the interrogation stop at mere consideration of muscle-fibre increase. In the series of cases already referred to Mr. Lawrence has found that the total kidney substance in some cases was far greater than the normal. In Case 42 the total weight was 19 oz.: in Case 46, 20 oz.: the pathological alteration of the kidneys in each case was minimal. In Case 42 there was albuminuric retinitis and hyperpiesis, death occurring from the accident of terminal infection. Case 46 died of "uræmia" associated with hyperpiesis. Increased "body weight" could not be held to be the cause of the increased weight of the kidneys, because Case 42, weighing 14 st. 2 lb. and showing a heart weighing 25 oz., revealed less total kidney weight than Case 46, weighing 11 st. 12 lb. only, and showing a heart weighing 39 oz.

Returning to the subject of idiopathic cardiac hypertrophy, we now know that this condition is a constant accompaniment of Hyperpiesia: formerly if kidney disease was found associated with cardiac hypertrophy, idiopathic cardiac hypertrophy became merely the hypertrophy of renal disease; but if no kidney disease was found, then there was little left in explanation of this phenomenon, and idiopathic cardiac hypertrophy held the field as a primary abnormality: or if the patient had happened to be a labourer or athlete, the qualification "athlete's or labourer's" hypertrophied heart was made.

If the reader's mind is by now prepared for the toxic explanation of hyperpiesis, then it remains to produce evidence which shall encourage such a view. Difficulties are met with at once, because there are so few pressor substances known. French writers have been at great pains to attribute hyperpiesis in part or entirely to the surcharging of the blood-stream with adrenalin. Just as Addison's disease is characterised by hypopiesis, so these are to be considered cases in whom the suprarenal bodies by over-activity have produced hyperpiesis. There can be no doubt that the suprarenal bodies are so placed that adrenalin could invade the circulation and produce a rise of pressure greater than the normal by hyper-

function of the suprarenal bodies, or as the result of some disturbance of the control of the usual charge entering the blood, such discharge requiring no naked-eye enlargement of the suprarenals themselves. Excessive function without hypertrophy has, however, proved a stumbling-block to many, and the fact that the suprarenal bodies are not hypertrophied in hyperpiesis has led workers to turn to other sources of pressor bodies. The pituitary body also yields a pressor substance, and what applies to the suprarenal bodies has been applied to the pituitary body: there is no close association between the enlargement of the pituitary body and the occurrence of hyperpiesis.

For reasons that are not far to seek, disorder of the kidneys has been considered to be closely associated with hyperpiesis, and cardiac hypertrophy, vascular changes, albuminuria and other phenomena have been considered to be renal in origin; and investigations have been made which, at any rate in some minds, have encouraged the belief that there is a direct relationship between hyperpiesis and kidney disorders. This subject will be referred to again in the next section.

Again clinical medicine has shown that some cases of hyperpiesis have been found to be temporary, lasting a few weeks or months and then passing off, and some writers are quite satisfied that this temporary form of hyperpiesis is amenable to treatment, and particularly to such treatment as is directed to the disinfection and clearance of the intestinal tract. It is not therefore without reason that poisonous pressor substances should be looked for in the disintegration of proteins in the intestine either as a result of putrefaction or of digestion.

SECTION IV

THE SEARCH BY EXPERIMENT FOR PRESSOR SUBSTANCES WHICH ACTING THROUGH THE BLOOD-STREAM COULD CAUSE A RISE OF BLOOD-PRESSURE

THE perusal of a paper by Swale Vincent and Sheen [1] on the effect of intravenous injections of extracts of animal tissues arouses interest because the writers appeared to have procured some evidence which favoured the idea, that when once the parenchyma of any particular organ as a result of various pathological processes reached the circulation, changes would take place in the degree of vascular tension. They made various preparations of organs of animals, including dogs', cats' and rabbits' tissues, and the procedure adopted for making "proteid extract" was the one followed in experiments to be presently mentioned - -a weighed quantity of fresh moist tissue was ground up with sand and to it were added three times as many cubic centimetres of saline solution as there were grammes of the tissues; the mixture was filtered and always used at once.

Proteid extracts of brain tissue.—They found that proteid extracts caused a rise, slight or marked, in five experiments. The rise pictured shows a persistence for at least ninety-two beats of the heart; in two experiments a fall occurred and in one injected with rabbit's brain the fall was a very pronounced one.

Proteid extracts of striped muscle tissue.—These usually gave a double effect, a short rise lasting presumably about four seconds, and fall for more than twelve seconds. A pure rise was noticed once, but never as marked as in the case of nervous tissue.

Proteid extracts of kidney.—They noted most frequently and characteristically the double effect, a rise and a fall. The next most frequent effect to occur was a pure rise: on one occasion a fall occurred and on another no change occurred whatever. The rise figured by these workers followed just after the injection and lasted about twelve heart-beats. They found that, speaking generally, there is in the case of kidney extracts, even more than with those of muscle or nervous tissue, distinct evidence of a pressor effect.

Proteid extract of liver.—In the one experiment performed by these workers the proteid extract produced a distinct fall.

Proteid extract of spleen.—A small but distinct fall was produced. A proteid extract of the intestine was tested once and gave a fall.

In the perusal of this paper the reader is struck by the observation that these

[1] *Journ. Physiol.*, London, 1903, vol. xxix. p. 242.

workers have frequently to refer to the fact that the results obtained were not uniform, and notably is this the case with their observations on pressor effects, so that they say the pressor effect seems to be less marked and of a more fleeting character, and consequently more difficult to obtain, than the depressor effect: the pressor effect may be easily missed unless the extracts are made in various ways and a long series of experiments undertaken. Strength of extract, dose given and stage in the experiment are all factors which are capable of determining whether a pressor or depressor effect is produced; the best way to obtain the pressor substance from any tissue is to extract the absolutely fresh tissue with physiological saline solution and, after thorough trituration and allowing the preparation to stand for a few minutes, to filter. A pressor or mixed effect should be obtained from these preparations. They conclude "that all glandular tissues and probably all animal tissues contain a pressor and depressor substance, the former being usually extracted by saline solution at ordinary temperatures, while the latter is extracted by boiling saline solution, which either destroys (wholly or partly) the pressor substance or masks its effect by producing more of the depressor substance." "The falls and rises of pressure are produced by vaso-dilatation or vaso-constriction of various vascular areas of the body." The writers were unable to say that any particular extract had a specific local effect referable to the homologous organ. A depressor substance is discoverable in the liver, spleen, testes, pancreas, ovary and lung. Other observers have found a depressor effect to be given by thyroid, thymus and pituitary extracts; even suprarenal extract when given in small doses exerts a depressor effect.

In connection with the subject of hyperpiesis, Swale Vincent and Sheen's results are most important in those particulars in which they are able to state that they have established a pressor effect of tissues when injected into the circulation. My own efforts at attempting to discover variations in the effects following the injection of tissues in various pathological conditions were followed merely by the observation that in practically all cases (seventeen in number) there was but one effect—namely, a depressor one; occasionally the injection of a preparation would produce a brief rise, much as does the simple injection of saline solution in some cases, though as a rule this latter solution generally causes a slight fall. However, a careful reperusal of Swale Vincent and Sheen's paper impressed me that the organs removed from individuals dying from different diseases were not fresh tissues, although keeping the bodies in an ice-chamber had prevented their putrefaction. Moreover, suspicions were aroused that possibly post-mortem softening might have so affected the reactions of the fresh tissues that, supposing any pressor substances had been present in the organs of the patients who had died, such active agent would have disappeared. At this stage I was very materially helped by Dr. Schryver, who pointed out to me a certain period subsequent to the removal of tissues from animals in which the tissues do not undergo chemical change. An appeal, therefore, was made to the effects of fresh tissues removed from cats and after preparation injected into others.[1]

[1] See *Lancet*, London, 1900, pp. 1295, 1375, 1455.

Mode of preparation.—An animal was killed under an anæsthetic, and with aseptic precautions the liver, the kidneys, the brain, the spleen, etc., were removed. The kidneys were stripped of their capsules, then split, and as much as possible of the pelvis and the neighbouring vessels were removed; the bile-duct and gall-bladder were cut away from the liver, and all the organs were washed in sterile saline solution. So much of each organ was weighed out in grammes, and to it were added three times the number of cubic centimetres of sterilised salt solution; this was then ground up with a small quantity of white sand which had been sterilised and washed in saline solution. After the preparation was thoroughly macerated it was pressed through fine-meshed sieves, thus completing the disintegration of the organ. The preparation was then centrifugalised and filtered through coarse filter-paper. The filtrate now took the form of a fine emulsion, and showed microscopically many fine granules of varying size. The preparations were injected into other cats, as a rule from within two to four hours, and in one case not for twelve hours, the preparation having been kept in an ice-box at from 8° to 10° C. The anæsthetic used was ether in every case, and care was taken, without the aid of morphine or curari, to secure deep anæsthesia. The ether was administered through a cannula inserted in the trachea. The blood-pressure was recorded from the right carotid artery. A cannula was tied into the right femoral vein for the purpose of injecting the extracts.

The first series of experiments carried out in the above way included those animals in which several different tissue extracts were injected into the same animal; the order of injection is given in Table VI.; the series consisted of eight experiments carried out on eight animals—Nos. 12, 22, 23, 25, 29, 31, 32 and 33A. No records of the experiments Nos. 12 and 23 are given; No. 12 was a curious example in which the animal failed to show any reaction—pressor or depressor—on the injection of any tissue or of saline solution alone. No. 23 was an example of an animal in whom the respiration was so irregular, quite apart from injection of material, that no attempt was made to carry out complete experiments. There are therefore six experiments left for consideration. The effects of injection of different organs upon the blood-pressure have been tabulated, and the analysis of the spleen and muscle effects shows that injection of spleen gave a rise of pressure on three occasions of 18 mm., 2 mm. and 3 mm., lasting respectively forty-five seconds, ten seconds and thirty seconds; a fall occurred in two cases of 4 mm., lasting from one to two seconds, and of 6 mm., lasting four seconds. Injection of muscle extract was practised twice; in one there was a marked fall of 38 mm., lasting four minutes twenty-eight seconds, and in the other a fall of only 4 mm., lasting one minute fifty-five seconds. The observations on the kidney, the liver and the brain were more numerous and are tabulated according to whether they caused a rise or fall (Tables VII. and VIII.).

It is obvious that though other organs than the kidney occasionally show a rise of pressure on injection, yet the rise is small and of short duration; whereas the kidney effect of a rise, though varying within considerable limits, is a striking feature, and the same may be said of the duration which such rise shows;

TABLE VI.—SHOWING PRESSOR OR DEPRESSOR EFFECTS FOLLOWING INTRAVENOUS INJECTIONS OF EXTRACTS OF FRESH ORGANS

No. of Experiment.	Date.	Weight of Kymograph Animal in Grammes.	Weight of Animal from which Organs were removed.	Anæsthetic, etc.	Nature of Extract.	Amount and Order of Injection of Extract of Different Organs.	Average Maximum Pressure immediately before Injection.	Effect on Pressure. Rise + or Fall − in Millimetres of Mercury.	Duration of Observation of Rise or Fall.	Remarks.
						C.c.	Mm.			
22	Jan. 23, 1906.	3625	..	Ether. Spontaneous respiration	Saline emulsion, 1 in 3. Used within 4 hours of removal	Spleen . . . 6	128	+ 18·0	45″	
						Muscle . . . 6	122	− 38·0	4′ 28″	
						Kidney . . . 6	122	+ 72·0	7′ 13″ at least	
						Liver . . . 6	144	− 16·0	2′ 50″ ,,	
						Liver* . . . 6	180	− 14·0	45″ ,,	*Between the first and second injections of liver extract suprarenal extract had been injected
						Kidney . . . 6	168	+ 24·0	4′ 35″ ,,	
						Spleen . . . 6	188	+ 2·0	10″ ,,	
25	Jan. 25, 1906.	..	..	,, ,,	Saline emulsion, 1 in 3. Used within 12 hours of removal. Kept at 80° C.	Spleen . . . 6	140	− 5·0	4″	
						Liver . . . 6	142	− 9·0	55″ at least	
						Blood . . . 6	136	+ 3·0	4′ 3″ ,,	
						Kidney* . . . 6	136	+ 30·0	30″ ,,	*Kidney rise preceded by fall of 22 mm.
						Liver . . . 6	166	− 7·0	4′ 30″ at least	
						Kidney* . . . 6	144	+ 36·0	30″ ,,	*Kidney rise preceded by fall of 32 mm.
						Liver . . . 6	176	− 6·0	30″ ,,	
						Kidney* . . . 6	170	+ 10·0	5′ ,,	*Kidney rise preceded by fall of 30 mm.
						Animal's own urine 6	178	− 78·0	2′ 50″ ,,	
29	Jan. 31, 1906.	3600	2716	,, ,,	Saline emulsion, 1 in 3. Used 2 hours after removal	Liver . . . 6	166	+ 6·0	30″	
						Normal kidney* . 6 (19·25 grammes)	160	+ 6·0	1′ 50″	*A fall was noticed immediately after injection of kidney extract, which was greater in the case of the healthy than in the scarred organ, probably owing to the presence of more urine
						Scarred kidney . 6 (8·2 grammes)	154	+ 24·0	3′ 50″ at least	
						Normal kidney . 6	178	+ 2·0	15″	
						Scarred kidney . 6	162	+ 10·0	2′ 30″ at least	
						Liver . . . 6	162	− 22·0	45″	
						Normal kidney . 6	130	+ 14·0	2′ at least	
						Scarred kidney . 6	136	+ 10·0	40″	
31	Feb. 2, 1906.	3580	2660	,, ,,	Saline emulsion, 1 in 3. Used 2 to 3 hours after removal	Muscle . . . 6	104	− 4·0	1′ 5″	
						Kidney . . . 6	100	+ 30·0	5′ 50″	
						Kidney . . . 6	130	− 24·0	55″	
						Liver . . . 6	132	− 8·0	1′ 30″	
						Brain . . . 6	122	+ 2·0	5″	
32	Feb. 6, 1906.	2760	2560	,, ,,	Saline emulsion, 1 in 3. Used 2 to 3 hours after removal	Liver . . . 6	184	− 8·0	10″	..
						Brain . . . 5	174	− 11·0	20″	
						Kidney . . . 6	160	+ 40·0	13′ 40″ at least	
						Brain . . . 6	192	− 18·0	50″	
						Brain . . . 6	184	− 11·0	20″	
						Kidney . . . 6	158	+ 16·0	7′ 30″ at least	
						Liver . . . 6	162	− 6·0	20″	
						Spleen . . . 4	156	+ 3·0	30″	
						Kidney* . . . 0	130	+ 16·0	1′ 30″ at least	*A fourth injection of 12 cubic centimetres of kidney extract gave only a slight rise, and a fifth of 6 cubic centimetres none at all
33A	Feb. 8, 1906.	3510	3200	,, ,,	Saline emulsion, 1 in 3. Used within 2 to 3 hours	Spleen . . . 4	162	− 6·0	1–2″	
						Brain . . . 6	160	− 12·0	25″	
						Kidney . . . 3	146	+ 22·0	3′ 40″ at least	

In Experiment 29 reference is made to the effects of normal kidney and to scarred kidney; the renal artery of the scarred organ was found to be much smaller than that of the healthy kidney.

no other organ has been noticed to have such an effect so frequently. The liver and brain show a much greater tendency to cause a fall of blood-pressure, and even then such fall is generally of very brief duration. One point to which it is necessary to draw attention is that in none of these experiments was the kidney extract injected first: the injection always succeeded that of some other organ, and it may be objected that it is possible that the rise of pressure following the injection of renal extract is due to some interaction of renal extract with some previous extract. Moreover, it may be thought that the renal extract is of a

TABLE VII.—SHOWING RISE OF PRESSURE AFTER INJECTION OF VARIOUS EXTRACTS

Experiment.	Maximum.	Duration.
	Kidney.	
22	72 mm.	7′ 13″
	24 ,,	4′ 35″
25	30 ,,	30″
	36 ,,	30″
	10 ,,	5′
29	6 ,,	1′ 50″
	24 ,,	3′ 50″
	2 ,,	15″
	10 ,,	2′ 30″
	14 ,,	2′
	10 ,,	40″
31	30 ,,	5′ 50″
32	40 ,,	13′ 40″
	16 ,,	7′ 30″
	16 ,,	1′ 30″
33A	22 ,,	3′ 40″
	4 ,,	1′ 40″
	1 ,,	25″
	Liver.	
29	6 mm.	30″
	Brain.	
31	2 mm.	Few seconds

different physical character and likely to cause a rise of pressure from some mechanical effect dependent upon the granules contained in the emulsion. As will be seen later, there is no reason to believe that either of these objections holds good. It is to be observed once again that these animals were simply under the influence of ether; this was so carefully administered that the respiration was maintained regularly. In another experiment, 33B, with ether anæsthesia and artificial respiration, the vagi were cut; an injection of renal extract then produced the exceedingly small rise of only 4 or 1 mm., lasting one minute forty seconds and twenty-five seconds respectively. So far as this one experiment is

concerned it must be stated that the second injection of an extract has on other occasions shown a less marked reaction than the first one. The slight rise, such as it is, merely suggests that the rise of pressure on injecting renal extract is due to a peripheral effect whereby the arterial pressure is raised.

At this stage it was necessary to reconsider the statement made by Swale Vincent and Sheen, that they had to *some extent* been able to corroborate the observations of Tigerstedt and Bergman,[1] inasmuch as they had found distinct evidence

TABLE VIII.—SHOWING FALL OF PRESSURE AFTER INJECTING VARIOUS EXTRACTS

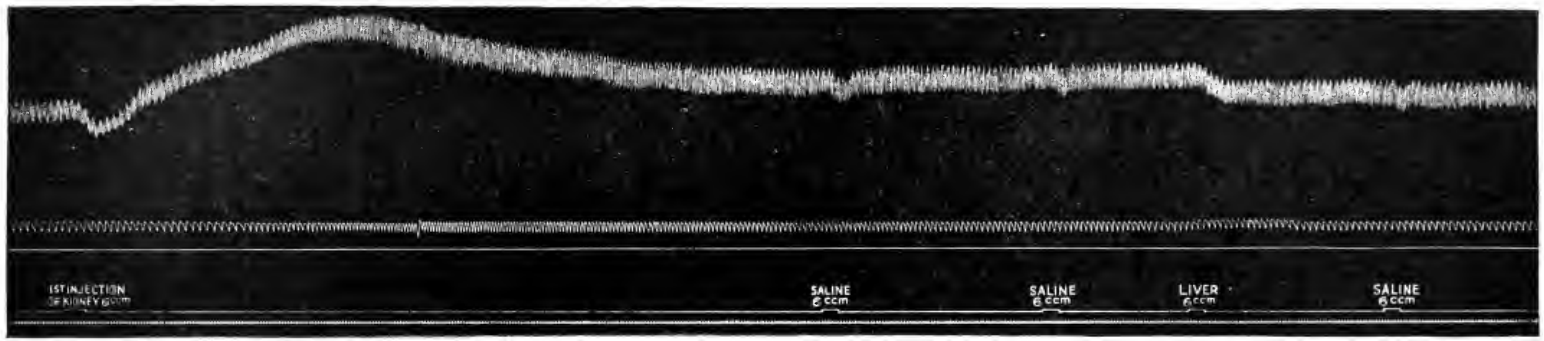
Experiment.	Maximum.	Duration.
	Kidney.	
31	24 mm.	55″
	Liver.	
22	16 mm.	2′ 50″
	14 ,,	45″
25	9 ,,	55″
	7 ,,	4′ 30″
	6 ,,	30″
29	6 ,,	30″
	22 ,,	45″
32	8 ,,	10″
	6 ,,	20″
	8 ,,	1′ 30″
	Brain.	
32	11 mm.	20″
	18 ,,	50″
	11 ,,	20″
33A	12 ,,	25″

In Tables VII. and VIII. the heading Maximum means the highest or lowest maximum point the blood-pressure reached respectively during the interval in which rise or fall occurred. The duration in Table VI. is qualified in many cases by the words "at least," because it was necessary in these cases to stop the kymograph to economise tracing-paper in order to get the whole series of observations on one tracing.

of the existence of a pressor substance in the kidney. The only figure given by Swale Vincent and Sheen in support of their findings shows a comparatively small rise and a small fall with a return to a level a little higher than the original height. In traces taken from my own series of animals it will be seen that there is often a fall and then the pressure rises and is maintained for some time. (For tracings see Fig. 10.) The different conditions of the animals must, however, be remembered. Swale Vincent and Sheen experimented on a dog, using A.C.E. mixture and presumably artificial respiration as well as morphine; whereas in my own

[1] *Skandinavisches Arch. f. Physiologie*, 1898, Bd. viii. S. 223.

EXPERIMENT 22



EXPERIMENT 22 (continued)

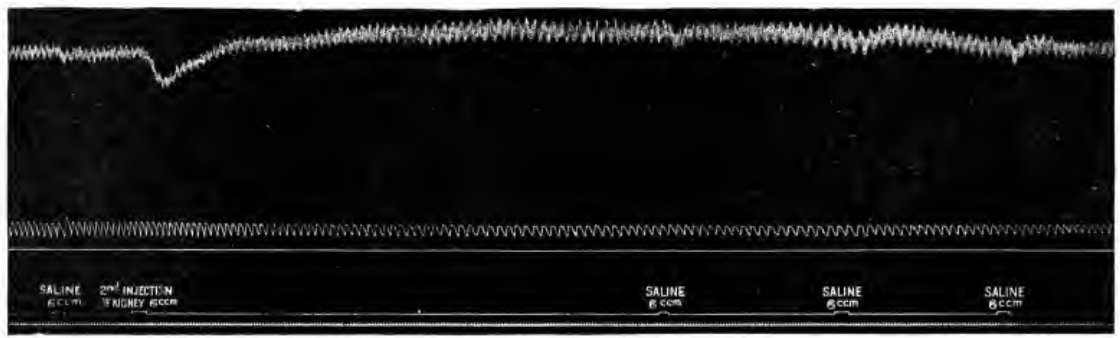
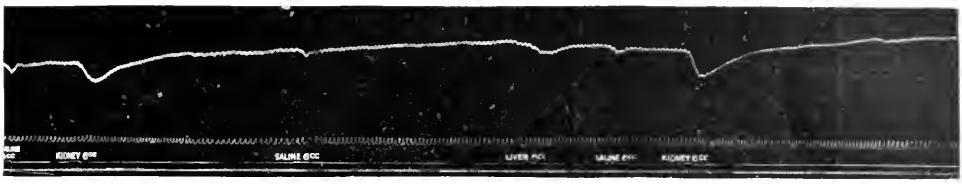
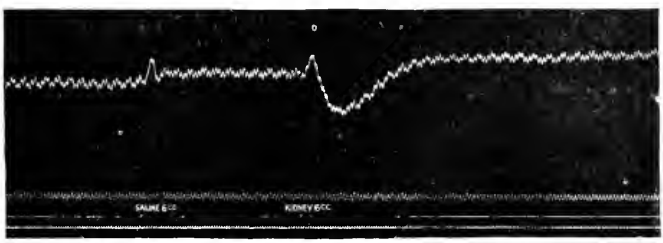


FIG. 10.—Showing the effect of experimental injection of renal extract. Compare with the injection of saline or liver extract.

EXPERIMENT 25



EXPERIMENT 29



EXPERIMENT 31

EXPERIMENT 32

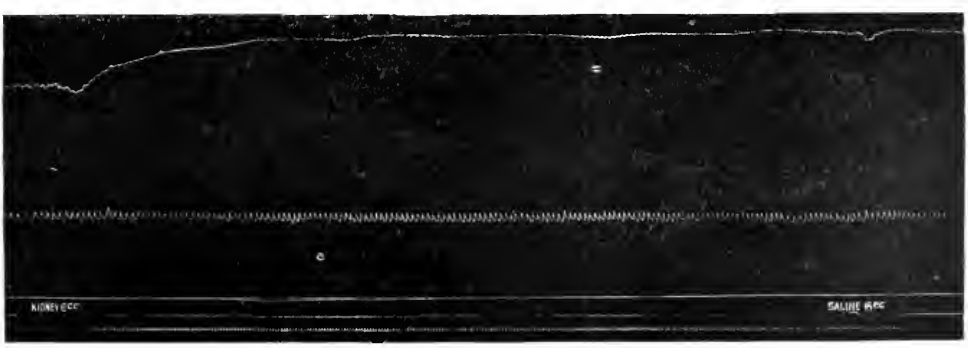
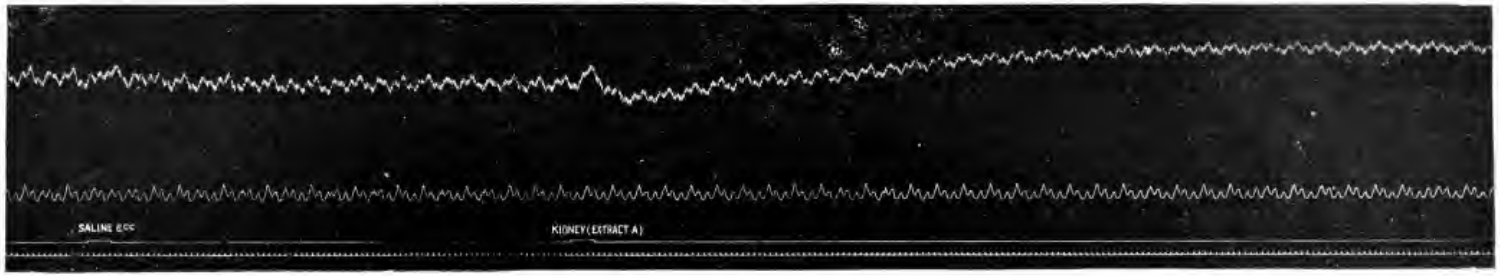


FIG. 10 (continued).

EXPERIMENT 41



EXPERIMENT 41 (continued)

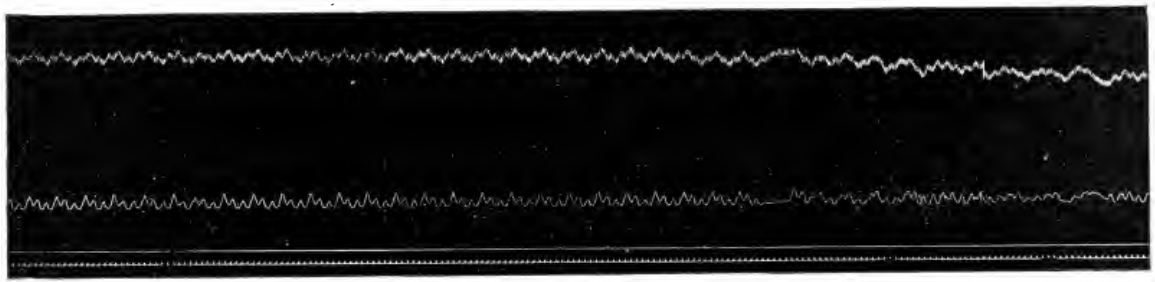


FIG. 10 (continued).

experiments cats were used, anæsthetised by means of ether with spontaneous respiration, and the effect, as already mentioned, is certainly much more striking.

Turning to Tigerstedt and Bergman's paper, it is found that these two workers had established results of a very different character from those given by Swale Vincent and Sheen, and I think that the results obtained in my small series of cats are in close agreement with the results obtained by Tigerstedt and Bergman, though in little else do I presume to compare my observations with those made by these workers. They had set themselves the task of elucidating the relationship between kidney and heart, being influenced by the teaching of Brown-Séquard on "internal secretion," and by the association existing between certain renal and cardiac diseases. Their first experiment was rewarded by an interesting result. Freshly excised rabbit's kidney was rubbed up with glass powder and physiological salt solution; the fluid obtained was then filtered and a few cubic centimetres were injected intravenously into rabbits. In a short time a well-marked and apparently protracted increase of arterial pressure was observed. In the first experiment within eighty seconds of the injection of 5 c.c. of the extract the maximal pressure had risen from 70 to 66 mm. before injection to 102 mm. after—*i.e.* an increase of pressure of about 50 per cent. had ensued; in a second experiment the increase after the injection of 4 c.c. was 25 per cent. within 100 seconds; in the third experiment there was an increase of 18 per cent. in sixty seconds. The investigation was further elaborated. They found that extracts which were prepared by boiling the fresh kidney with water or extracts prepared from the boiled kidney by means of cold water were inactive; moreover, by boiling or heating the fresh extract the pressor effect was destroyed. An important discovery was that alcohol, either absolute or of 50 per cent. strength, was quite unable to extract from the preparation any active material. They were also able occasionally, but not always, to demonstrate that diluted glycerine extract had a definite pressor effect; the failures to produce a rise of pressure were attributed to the well-known depressor effect of the glycerine, and in one experiment it was thought that the first injection of glycerine extract had produced a fall only. A second dose was given before the true effect of the first one had shown itself, and after 140 seconds the pressor effect of the second dose was found to have developed so that the blood-pressure was 16 per cent. higher than originally.

One of the objections to the use of the extract which has been injected into the series of cats already referred to is that the material injected was a coarse emulsion, and that until this emulsion could be made to yield a soluble substance capable of exerting a pressor effect the results obtained could not be quite convincing. Tigerstedt and Bergman have, however, succeeded in obtaining a solution of the active material which can be quite freed from any granular contents. The kidney is rubbed up with absolute alcohol and filtered; the precipitate is dried in the air at room temperature and is then extracted with salt solution. One to 2 c.c. of this extract exert as great a pressor effect as the fresh preparation: the active substance is not destroyed by alcohol. They speak of this extract as "Extract A." If it is boiled or heated in a water bath this extract loses its

properties, but exposure to a temperature of from 54° to 56° C. does not apparently disturb the pressor effect. The pressor substance, to which these workers give the name of " renin," is not *dialysable*. From these various reactions it may be concluded that renin is a substance *sui generis*, and that the effects produced on the blood-pressure are not due to any of the crystallisable substances which are excreted in the urine. (Riva-Rocci had also failed to demonstrate a pressor effect in any constituent of the urine.) A further interesting observation was made by these workers that " renin " was present only in extracts made from the *cortex of the kidney*, and not at all or only to a slight extent in extracts of the *medulla*.

These two workers give a long list of all the experiments they carried out in which the nervous system was left intact and excision of the kidney had not been carried out in the animal into which the injections were made. The list includes twenty-three animals (rabbits), and the number of injections was fifty-three in all: on fifty occasions the effect on the rise of blood-pressure was positive, and in three cases only there was a negative effect ; but it is to be observed that in each of these three cases injections had already been made with positive effects, and it is known that the effects of the latter injections are frequently less marked than earlier ones. A remarkable feature of the effects of injection is the long time during which the effects last. After a somewhat rapid and transitory fall of pressure the arterial pressure begins to rise and reaches gradually a maximum within an interval of from one to two minutes. The blood-pressure then sinks slowly, but in certain circumstances remains for twenty minutes at a higher level than before the injection. The degree and duration of the rise are apparently independent of the amount of extract injected, except in those cases in which the amount of injection is very small, when it will be found that the rise is less than in doses which are a little larger. In repeated doses the extract exerts in some cases an effect as large as in the first injections, but in other cases, and apparently in most, the influence of the second dose is less than is that of the first one. The absolute rise of pressure in the experiments in which a watery extract was used is in general greater according as the initial pressure of the animal is lower. The experiments with " Extract A," however, show in this particular less regular effects, and Tigerstedt and Bergman explain this on the ground that the " Extract A " is not always equally rich in renin and that various individual animals vary in their reaction to its effects. These two authors then proceed to analyse the effects produced. They found that the changes of pulse frequency after injection of renin are not great, and it may be concluded that the pressor effects exerted by renin cannot be dependent on alterations in pulse-rate. The pulse changes are much more likely results rather than causes of the rise of pressure. Division of the cervical nerves did not interfere with the effects met with after injection of the " Extract A." Nor does it appear likely that the renin acts upon the heart, for they found that preparations which in an intact animal produce the usual effects are quite unable to show any effect on the isolated surviving rabbit's heart. Nor was it possible to attribute the effects to changes in the chief vaso-motor centre, for the effects were present when the cervical cord was cut and also when the cord

was cut at the level of the fourth dorsal vertebra. Nor were the effects due entirely to action on the spinal vaso-motor centres, for destruction of the whole spinal cord by means of a sound failed to abolish the effects completely: they could not, however, exclude some possible effects due to action on the vaso-motor centres of the spinal cord, and this was shown by the fact that when both vagi were cut and an injection of 6 c.c. of "Extract A" had been made, stimulation of the right depressor nerve caused a fall of pressure. This same experiment also showed that the effect was not upon the musculature of the blood vessels, and it will be remembered that Oliver and Schäfer used this mode of experimentation to prove that extract of suprarenal substance did act on the musculature of vessels. The net result of these observations on the analysis of the effects produced by injection of "Extract A" was to show that fresh renal extracts produce rises of pressure by acting on the peripheral nerve centres as well as possibly on the spinal cord. (See Fig. 11.)

Finally, Tigerstedt and Bergman consider the question of the fate of renin when it enters the circulation normally. As already stated, under favourable conditions the rise of pressure in intact animals lasts almost twenty minutes. If, however, the kidneys are removed the pressure is raised for a very considerably longer period of time, but eventually even in these cases its effect wanes. From this it may be concluded that renin is got rid of from the body partly by the kidneys, but also that it is partially destroyed by the tissues or is possibly got rid of by the bowel.

I have quoted the observations made by these two workers in much detail, because I think their discovery is so important to pathology, not only in the study of disturbed action of the kidneys, but in the study of the subject of auto-intoxication in general. So careful and so exacting have they been in their work that it is difficult to offer criticisms which would be of great weight. There are some points, however, upon which we require more information. The first is that there is no mention whatever of the anæsthetic used—whether it was of the nature of chloroform or ether or of morphine. It is therefore possible that the same criticism may be offered upon their work as upon my own—namely, that the effects were not obtained in an animal when placed under the most favourable conditions for the investigation of problems connected with the vaso-motor system. The writers expressly state that in the twenty-three cases in which fifty successful injections were made—*i.e.* were followed by a rise of pressure—the nervous system was intact; possibly atropine was therefore not administered. Another point is one which is of great importance—they apparently had few failures. In one case already referred to in my own list it will be remembered that the animal failed to respond to any injection, and in another respiration was so faulty without injection that the experiment had to be abandoned. In another case the injection of renal extract was followed by a very notable fall of 20 mm., which lasted fifty-five seconds; in the light of Tigerstedt and Bergman's work it may be that this was due to some other influence than that exerted by the renal extract or that some change had taken place in the extract, especially

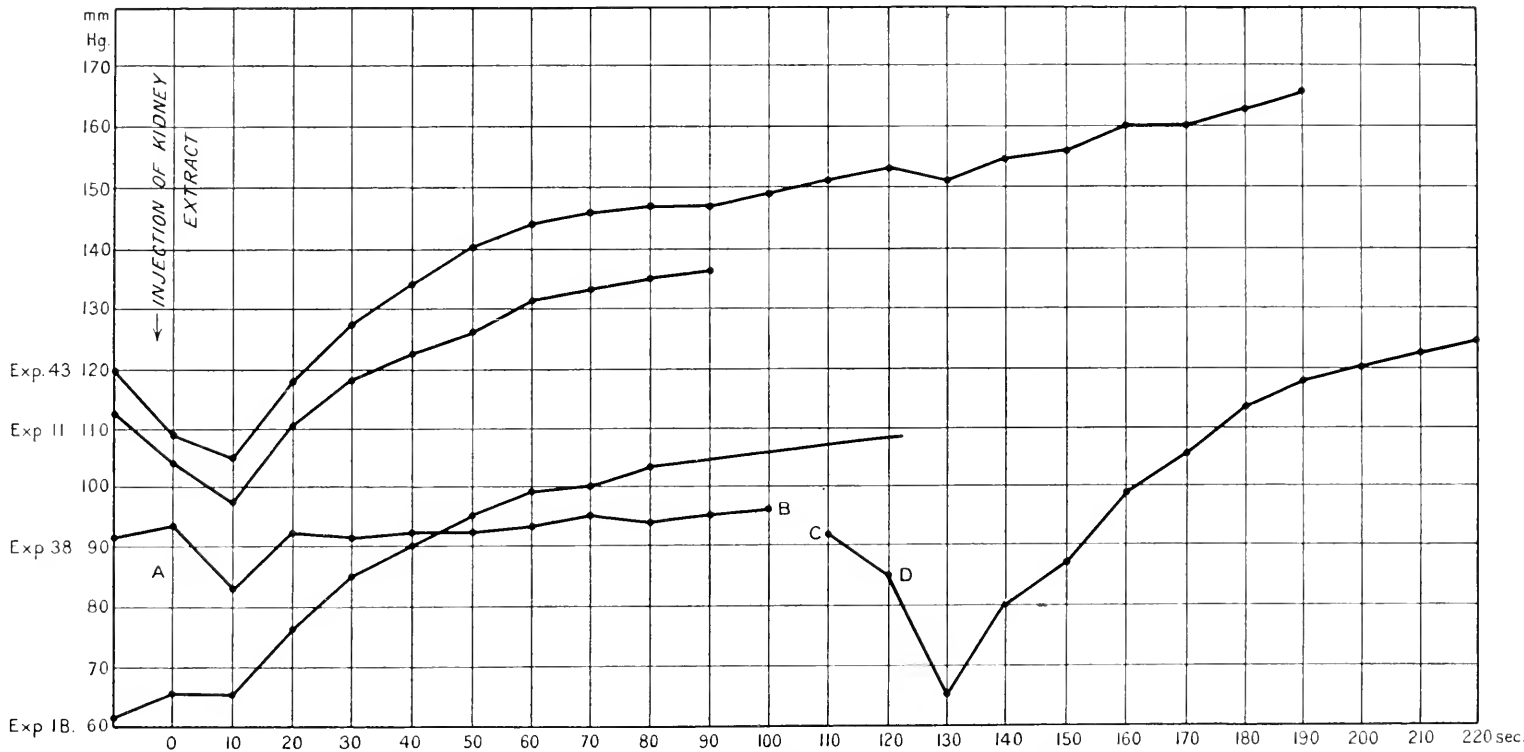


FIG. 11.—Diagram (after Tigerstedt and Bergman) showing effects of experimental injection of renal extracts upon blood-pressure. In Experiment 38, extract of the medulla of the kidney was injected at A. Between B and C the pressure did not rise, and after 120 seconds was found to be at C. At D extract of the cortex of the kidney was injected and the subsequent rise of blood-pressure is shown.

as an earlier injection of the same extract in the same animal had given a rise with a maximum of 30 mm., lasting five minutes and fifty seconds. It seemed as well, however, to endeavour to secure results under the most exacting physiological conditions possible, and so a limited number of further experiments were carried out, using renal extract for injection purposes prior to the injection of any other preparation.

The analysis of these results shows that on three occasions when the experiment was carried out, as in my first series, under the influence of ether only with spontaneous respiration a fall succeeded the injection of renal extract. A fall lasted four minutes and sixteen seconds, and the lowest maximum pressure was 4 mm. below the original in Experiment 37. In Experiment 39 the fall was a very great one and reached 50 mm., lasting fourteen minutes at least. In Experiment 42 a similar fall of 50 mm. occurred, lasting one minute, fifty-one seconds ; the animal used in this experiment must, however, have been under abnormal conditions, for the division of both vagi was not followed by a rise of blood-pressure ; variations of the distribution of inhibitory fibres in the vagi of the cat are known. In Experiment 38 ether anæsthesia was carried out as well as artificial respiration ; the very anomalous result was observed that the first injection was followed by an unusual fall of 75 mm. and the second by a rise of 1 mm.

Turning now to the results obtained when anæsthesia was procured by the administration of ether and morphine, respiration being carried out artificially, a rise of pressure followed the injection of renal extract on four occasions (Experiments 36, 38B, 41 and 42B). No rise and even a fall occurred in three experiments (Experiments 38B, second injection, 40A and 41, second injection).

Another condition under which the injection was made was to administer ether and morphine or curari, to carry out artificial respiration, and to cut the vagi. A rise of pressure followed the injection of renal extract in three cases (Experiments 35, 38C and 39B). A fall occurred in two cases (Experiments 38A and 40B).

These results are obviously unsatisfactory, for although the majority give some support to the view that there is a pressor substance extractable from the kidney, a good proportion of cases show the reverse. It may, however, be conceded that the much more uniform effects produced when the animal is intact and adequate anæsthetisation has been produced by ether give a better idea of the effects produced by renal substance than when various operative measures, etc., have been carried out as well. Considering the frequency with which Tigerstedt and Bergman obtained pressor results with their preparation " Extract A," it may be that further experiments carried out with this preparation under conditions of a more exacting nature—for example, anæsthesia under ether or chloroform and morphine—will give more uniform results. As already stated, the two workers referred to do not say what anæsthetic was used, and it is not very clear how they prepared " Extract A," for the amount of absolute alcohol added to the original kidney substance is not mentioned, nor is reference made to the amount of saline solution with which the dried residue was rubbed up ; it was surmised

that for the preparation of "Extract A" five times as many cubic centimetres of absolute alcohol should be added to the kidney pulp as there were grammes of that substance. The residue left after the removal of the alcohol in a desiccator was rubbed up with a 1 in 3 saline solution.

Further confirmatory observations on the pressor substance present in the kidneys were made in 1909 by Bingel and Strauss.[1] As a result of their experiments on the introduction of preparations of kidney substance by intravenous injections they concluded that renin differed from adrenalin in its more prolonged effect in producing a rise of blood-pressure. The influence of renin was not affected by section of the vagus or of the sympathetic or by destruction of the spinal cord, nor by the extirpation of the kidneys or suprarenals or by removal of the liver. Renin acts probably at the periphery on the musculature of the arteries. They confirmed the view that a pressor substance is present in the kidneys, that it is possible to isolate this substance, and that this fact was not without significance for the explanation of rise of blood-pressure in those suffering from kidney disease, and especially from the contracted form of kidney disease. Their autolysed preparation of the juice of fresh kidney substance was one which contained no salt, and but a small amount of protein. In 1910 Bingel,[2] with another fellow-worker, Claus, again confirmed the presence of renin in the kidney. They were also able to show that in contradiction to adrenalin, renin on injection caused an enlargement of the kidney under plethysmographic observation. They also found that renin on injection caused contraction of an extremity and produced diuresis.

It seems therefore established experimentally that a substance is present in the normal kidney which is capable of producing a rise of blood-pressure when injected into other animals.

Has this fact any bearing upon the subject of Hyperpiesia?

With the extended study of the forty-seven clinical cases in mind, with its extraordinarily varied pictures of the condition of the kidneys found post-mortem—pictures which at one end of the scale showed organs scarcely different from the normal, and probably not at all different from the kidneys of patients who during life showed no hyperpiesis (although this particular point forms no part of the inquiry) and at the other end showed organs which were seriously diseased—indeed showed the ordinary appearance of granular kidneys, the answer must be a qualified one. In common with many other observers I felt in 1906, with a limited number of cases of hyperpiesis whom I had studied post-mortem in view, that as so many of the cases showed extensive kidney disease there probably was some very close connection. It seemed a reasonable view to take that although it had never been found that in health the kidneys delivered renin into the circulation, it was possible in disease that they succeeded in doing so. It was a tempting theory, for it was in those cases in whom the cortex (so rich in renin) was shrivelling that the disappearing kidney substance gained access to the circulation. The present study still gives room for such a view, despite the fact that no one has

[1] *Deutsches Arch. f. klin. Med.*, 1906, xcvi. S. 476. [2] *Ibid.*, 1906, c. S. 412.

succeeded in proving that the sera of people suffering from hyperpiesis have a pressor effect in excess of the sera of healthy individuals—possibly this is because the renin is rapidly fixed by the musculature of the vessels and is not free in the blood-stream.

The fact remains, however, that hyperpiesis was present in cases in whom the kidneys were to all clinical intents and purposes normal.[1] If the kidneys were still to be looked upon, even in these cases, as the source of the rise of pressure, then it would mean that in these cases the kidneys yielded to the circulation, renin, without suffering any change in their architecture ; in other words, that the kidneys in such cases yielded what might be called a pathological internal secretion —a contradiction in terms, and therefore inadmissible. It is impossible, however, to ignore the fact that kidney cells are constantly disappearing from the kidney and are being replaced by fresh ones, which would help to explain the difficulty that although the kidneys were yielding this substance to the circulation, and so causing a rise of pressure, they could continue to do so (by regeneration of kidney cells) during long periods of time—even years. Moreover, it cannot be gainsaid that the kidneys in many of these cases are undergoing hypertrophy in numerous small sites, thereby helping to make up for the loss at others, and that in some cases they show that hypertrophy is universal and apparently not accompanied by any areas of atrophy and loss.

There is, however, no necessity to relegate all cases of hyperpiesis to the effect of renin, for it is possible that other substances of quite different origin are pressor in action and capable of accounting for hyperpiesis and only await discovery, and these will share, or possibly appropriate to themselves, the whole responsibility for Hyperpiesia. Indeed the existence of such bodies has already been demonstrated : it may be that they or allied bodies are responsible for hyperpiesis to the exclusion of the kidney in some cases, or in all. It has formed no part of this study to follow cases of normal or subnormal blood-pressure and collect evidence on the configuration of the kidneys in them ; but it has long been known that cases of shrunken kidneys (or even granular kidneys) occur in whom no cardiac hypertrophy is present, as shown at the post-mortem examination.[2] We still want, however, observations at the bedside which show that these self-same cases never showed during life any evidence of hyperpiesis : when this has been established then the view that renin may be the cause of some of the cases of hyperpiesis falls to the ground, and it would have to be admitted that hyperpiesis is in no case a function of kidney disease. Hyperpiesis would have to share the fate of cardiac hypertrophy (independent of valvular disease), of albuminuria (independent of renal disease), of albuminuric retinitis (independent of renal disease), of renal asthma and of many of the features of uræmia (independent of kidney disease), and in common with these manifestations be considered to be something quite independent of the particular form of disease the kidneys may show in each case. It seems quite clear that if all connection

[1] Also Janeway, *Am. Journ. Med. Sc.*, Phila., 1900, vol. i. p. 772.

[2] See also Geoffrey Evans, *Quart. Journ. of Med.*, vol. xiv. No. 55, p. 245.

between hyperpiesis and kidney disease must be abandoned, then the fabric of much of our present-day beliefs in the association of various signs and symptoms of renal (?) disorder with actual renal disease must also be abandoned—a view which, though heterodox, is reasonable. The only remaining certain sign of destruction of the kidney is one which arises when the whole, or almost the whole, of the kidney has undergone atrophy (as in Case 1) ; and this sign is anuria. All other signs must be looked upon as expressions rather, not of the failure of the kidneys to act, but of the effect upon the body as a whole of toxic substances which have reached the circulation from some site other than the kidney, and which may, or may not, be responsible as well for the damage to the kidney, and as a result of this for the retention of metabolites which experiment has shown so far not to be responsible for the effects spoken of as uræmia. Uræmia itself would then be but an expression of the toxic effects of poisons which are of pre-renal origin.

In this connection the lessons taught by eclampsia will not be without their points, for in this condition a poison or poisons exist in the body of the pregnant woman which are capable of provoking all the manifestations of " uræmia "—even death—and the post-mortem examination may show changes in the parenchyma of the liver as well marked as, or better marked than those in the kidney. Removal of the contents of the womb may be followed by complete recovery from the toxic symptoms, including changes in the retinæ. It is clear that pathologists who have studied eclampsia have found themselves in much the same difficulties as those who have studied the association of hyperpiesis with the kidneys, but they have subdivided cases of eclampsia into those connected with grave structural changes in the kidney and those in whom no change has been found, or if any has been found it is of an acute degenerative nature, allied to the degeneration which may also be found in the liver of these cases. They discuss therefore pregnancy complicated by " uræmia " and structural unrecoverable changes in the kidneys, and pregnancy complicated by eclampsia with recoverable toxic changes in the kidneys of variable degrees of intensity. In the same way hyperpiesis may occur with structural unrecoverable changes in the kidneys ; or it may occur with no changes in the kidneys, or with changes which are slight and of a purely toxic character—these latter cases would agree with those which Sir Clifford Allbutt has designated cases of Hyperpiesia. It would seem, however, more reasonable to say that " uræmia " (and eclampsia) is a purely toxic condition and may prove fatal in some cases and may be recoverable from in others, and when an opportunity presents itself for a post-mortem examination it may be found that the kidneys are quite normal or show slight or extensive evidence of purely toxic parenchymatous change, or indeed may show coarse naked-eye manifestations of permanent structural alteration with fibrosis, etc. It must not be thought that this view insists that the latter changes are merely coincidences, but that the toxic causes which may in some cases produce but slight necrotic changes in the parenchyma may in others through a long period of activity of the toxins in small, more manageable doses, lead to the disfiguration of the kidneys met with in the

Small White Granular Kidney, or supposing at any time the toxic effect is so great and so rapid in action as to lead to what we know clinically as a case of Acute Parenchymatous Nephritis or of Chronic Parenchymatous Nephritis which, not proving fatal, gradually leads to the Secondary White Kidney or Contracted White Kidney. In other cases again the toxic agent may be replaced by other toxins which produce vascular disease in the kidney, giving rise to the red granular kidney ; or both sets of toxic agents may operate at the same time and produce contracted kidneys showing vascular and parenchymatous changes. Whether the kidney is granular, fibrotic and small, or granular, fibrotic and large, showing some or no vascular disease, will depend upon the power of the kidney to regenerate in small numerous areas or universally throughout ; in this way the varied pictures will be produced both of the extreme and intermediate types met with in this series of forty-seven cases. It is indeed allowable to speculate that the effort of the kidney to respond favourably to the task of excluding these toxic agents may lead to the enormous hypertrophy of the kidneys pointed out by Mr. Lawrence in some of these cases (*vide* p. 123).

An objection may be raised to the view just expressed, according to which it may be argued that supposing " uræmia " (and eclampsia) and such changes as are present in the kidneys (including those which are due to vascular disease) are all due to the operation of toxic agents present in the blood, then hyperpiesis and other attendant manifestations should intensify towards the end of life in those cases like Case 1 in which it is found post-mortem that the kidneys are totally destroyed owing to the fact that the toxic agents have accumulated in the system. It is, however, not claimed that the kidneys are the route, or the only route, by which such agents are extruded: moreover, the various slight uræmic manifestations met with in Case 1 had increased towards the end of life until death ensued : it is true that the hyperpiesis did not increase, and indeed so far as the chart shows had never been extreme, but it was maintained at a fairly constant level. It must again be pointed out, however, that in many other cases the hyperpiesis gave place to a normal or subnormal pressure before death : this, however, has been explained in many cases by the occurrence of terminal infections which clearly in some of the cases were contemporaneous with the falls of pressure—infection caused the blood-pressure to fall without showing change in pulse or temperature (see Chart 51). Some of the charts show that death occurred from infection with the maintenance of a high degree of hyperpiesis : hyperpiesis occurred with rapid, feeble pulse at the very end of life, and blood-pressure observation became at last impossible to register.

Until, however, more investigations have been carried out to prove the contrary, it is more reasonable to suppose that some cases of hyperpiesis may be due to a pathological internal diversion of renin, although other " uræmic " and eclamptic manifestations may be due to circulating toxins of non-renal origin.

Hyperpiesis may be present in patients who are entirely free from any other symptoms of a toxic character. Such patients may die later on from some cause

not directly connected with hyperpiesis such as is shown in this series, *e.g.* from carcinoma of the stomach, from apoplexy, pneumonia, etc., and the kidneys may be found normal. In these patients the toxicity of the blood produced hyperpiesis and attendant cardiac hypertrophy and tortuosity of the blood vessels.

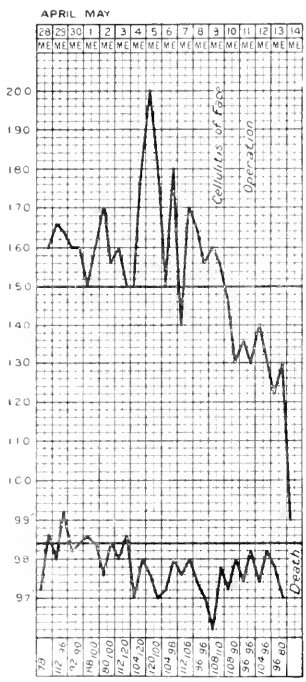


CHART 51.

Chart 52 was drawn up from the blood-pressure readings of a woman under the care of Mr. Gwynne Williams: she was suffering from hydronephrosis and from hyperpiesis. The blood-pressure readings were noted before and after operation for removal of the hydronephrotic kidney, and the remarkable change, apparently due to the removal of the diseased kidney, from a state of hyperpiesis to one of normal blood-pressure which was maintained during the rest of her stay in the hospital is a strong argument in favour of the view that in her case at least the kidney was closely associated with the occurrence of the hyperpiesis: whilst the kidney was present in the body hyperpiesis was a feature: when it was removed the blood-pressure became, and remained, normal.

Frequent observations have been made which have shown that cases which clinically appeared to be ones of acute or subacute parenchymatous nephritis may show hyperpiesis for a week or two, and with the recovery from the albuminuria and all symptoms and signs the pressure has become normal or subnormal. It is true that such cases may be examples showing that hyperpiesis, parenchymatous nephritis and attendant albuminuria may all be due to some pre-renal toxic condition of the blood of a temporary character, but they may be exemplifications of the fact that the kidneys damaged by a circulating toxin react by a discharge of renin into the system causing the hyperpiesis. (See Chart 53 showing the blood-pressure readings taken from a case of acute nephritis which recovered.)

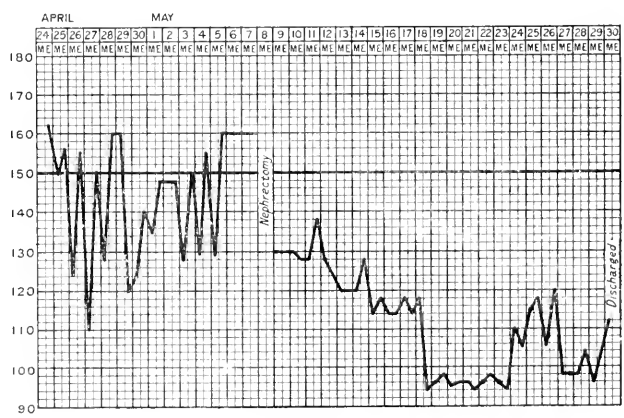


CHART 52.

The following facts also give good reason for believing that some cases of

hyperpiesis may owe the hyperpiesis to renal disorders. In the series of cases already studied in detail it is learnt that :

(*a*)	64 per cent.	of the cases of hyperpiesis showed distinct renal symptoms.
(*b*)	54 ,,	,, ,, ,, ,, albuminuria constantly.
	42 ,,	,, ,, ,, ,, albuminuria occasionally.
(*c*)	40 ,,	,, ,, ,, ,, albuminuric neuro-retinitis.
(*d*)	60 ,,	,, ,, ,, ,, casts in the urine.
(*e*)	over 70 ,,	,, ,, ,, ,, changes in the Malpighian corpuscles and tubules.
(*f*)	38 ,,	,, ,, ,, died of uræmia.
(*g*)	42 ,,	,, ,, ,, showed kidneys underweight.

In this study of forty-seven cases of hyperpiesis, it has been found that death from uræmia occurred in nineteen cases and grave kidney disease was found in sixteen cases, but no kidney disease in three. From these facts the deduction may be made that uræmia—a condition for which no satisfactory explanation has ever been found, so far from being dependent upon faults of the kidney, is an expression of the effects of some pre-renal toxic blood state entirely independent of the kidney. For though kidney change was present in such a large proportion of the nineteen cases who appeared to die of uræmia, thereby supporting the view that uræmia is in some way caused by kidney disease, kidney disease was not present in all of the nineteen cases, and, moreover, similar grave kidney disease was found in some of the remaining twenty-eight hyperpiesic cases who did not die of uræmia. Clearly death from uræmia was impossible in the three cases, and by deduction from this, improbable in the sixteen cases. It was more probable that the uræmia in all the nineteen cases was due to some pre-renal cause operating in the blood-system. Hyperpiesis, which is an accompaniment of so-called uræmia, being present in all of the above cases of death from uræmia, occurred also in all the remaining twenty-eight cases who did not die of uræmia. Hyperpiesis was a constant accompaniment of uræmia, but uræmia was not a constant accompaniment of hyperpiesis.

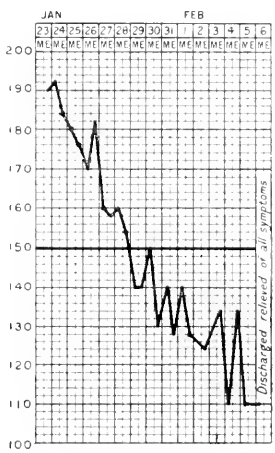


CHART 53.

There was grave kidney disease present in some of these twenty-eight cases, but in six of them (Cases 2, 12, 26, 32, 34 and 45) the changes in the kidneys were so slight as to be negligible. Therefore hyperpiesis in all cases showing this sign may be, like uræmia, due to the effect of a blood-poison, *i.e.* of a pre-renal cause, but it cannot be logically concluded, as in the case of uræmia, that hyperpiesis cannot be due to kidney disease because renin is as it were ready to hand and because of the frequency with which hyperpiesis is found in acute renal disease.

Hyperpiesis may have a dual site of causation : it may have had a seat of causation in the kidney in sixteen of the cases of death from uræmia and in the twenty-two cases of death from some other cause, all of whom showed grave

kidney change, and may be aptly described as "renal" or "nephræmic" hyperpiesis, and it may have had a seat of causation in the blood-stream in the remaining three of the uræmic deaths, and in the remaining six of the non-uræmic deaths, all of whom showed negligible changes in the kidney, and in this case may be described as Idiopathic or Essential Hyperpiesis, or by an extension of the use of Sir Clifford Allbutt's term—Hyperpiesia.

The fact of the existence of "renin" supports the possibility of the existence of "renal" or "nephræmic" hyperpiesis. How can support be found for the view that Essential Hyperpiesis or Hyperpiesia is toxic in origin, and is due to some pre-renal cause?

Up to the year 1906 chemical investigation had not revealed any substance derived from the disintegration of proteins capable of exerting a pressor effect.

One well-established form of treatment for Hyperpiesia has been accepted, namely, that of the use of aperients, of intestinal disinfectants such as calomel, and the simplification of the diet. In short it had been suspected that the intestinal tract yielded substances which were capable of causing hyperpiesis, despite the fact that none of the products of digestion of proteins had ever been shown to be pressor in their effects. In the year 1906 Abelous, Ribaut, Soulié and Toujan discovered that an extract of putrefied horse-meat raised the blood-pressure when injected intravenously, and that this was due to a chloroform-soluble base which was subsequently proved by Rosenheim [1] to be also present in placental tissue which had undergone putrefaction. Barger and Walpole [2] discovered that putrid horse-meat also yielded a substance which was soluble in water and produced pressor effects. The chloroform-soluble base is isoamylamine, and the base discovered by Barger and Walpole which was much more actively pressor was established by them to be p-hydroxyphenylethylamine, which is identical with the base derived by the elimination of carbon dioxide from tyrosine. They also showed that there was a third pressor body present in the extract of putrid meat, namely, phenylethylamine. Dale and Dixon [3] described in detail the physiological action of the pressor amines produced during putrefaction. These investigations lead to the conjecture that pressor amines are normally formed by putrefaction within the intestines and are absorbed from it. Probably these substances in health are prevented from entering the general circulation in quantities sufficient to raise the blood-pressure, by the action of the liver.

There can be little doubt that these investigations point to the possibility that there are other claimants for the causation of hyperpiesis, and that putrefaction in the intestines, and even prolonged peptic digestion (shown by Langstein to yield p-hydroxyphenylethylamine), may be responsible if the liver fails to act normally, not only for the rise of blood-pressure in cases in whom the kidneys are normal, or practically so, but even in those in whom the kidneys are, as it were, independently diseased. In other words, it may be that renin does not operate in these latter cases at all.

[1] *Journ. Physiol.*, London, 1909, vol. xxxviii. p. 336.
[2] *Ibid.*, p. 341.
[3] *Ibid.*, 1909–10, vol. xxxix. p. 25.

There remain several other clinical phenomena besides hyperpiesis connected with the subject of Hyperpiesia which present difficulties in their explanation.

The study of this series of cases of Hyperpiesia has confirmed what is well known, namely, that Hyperpiesia may exist and yet the patient during life may reveal little or no symptoms of the disorder: indeed, many persons have been found to reveal Hyperpiesia and have expressed their surprise that they are suffering from any abnormality: even further clinical examination has failed to show any of the signs other than hyperpiesis—no signs or symptoms of cardiac hypertrophy and none of vascular change—phenomena which, though developed later than hyperpiesis, may be looked upon as early manifestations of the disease. Moreover, cases of apparent normal health occur in whom death has taken place suddenly, as for example from apoplexy, anuria, cardiac failure (from disease of the muscle) or pulmonary œdema, and yet the post-mortem examination has established the changes so regularly found in cases of Hyperpiesia. In other cases death has been gradual and was dependent upon carcinoma, pneumonia, pleurisy, pericarditis, cellulitis, etc., and again at the post-mortem examination hyperpiesic changes have been found to have been in existence though playing no part in the actual death. In yet other cases death has occurred from what may be considered later manifestations of Hyperpiesia, *e.g.* from coma or from epileptiform fits: or the patient may have sought help for œdema in the form of dropsy, serous effusions or slowly developing œdema of the lung, blindness, hemiplegia, etc.

This study would in no way be complete were such phenomena not considered etiologically. It is notorious that the pathology of these complications and sequelæ is enwrapped in as much obscurity as hyperpiesis itself. Explanation must be found which shall be in harmony with the principle already enunciated, that the common causes are as a rule pre-renal in site and only exceptionally if at all renal in site and origin.

Terminal infection.—It has already been shown that death in Hyperpiesia is frequently due to the effect of infection. Are there any facts which help to show why Hyperpiesia predisposes to infection? There is only one common clinical experience which will help in this direction, namely, that there are other diseases quite different in nature from Hyperpiesia which prove fatal by terminal infection—cases of diabetes mellitus may die of pneumonia, or from pulmonary tuberculosis; cases of leucocythæmia may die from empyema or pneumonia or pericarditis, and cases of cirrhosis of the liver succumb to pulmonary infection. Such experience has led to the crystallisation of an axiom that any primary disorder not necessarily due to infection may in the last stages develop infections which are the cause of death. It is thought that the primary disorder so lowers the power of resistance to infection that inflammation of various tissues occurs the more readily. Hyperpiesia is apparently no exception to this rule. There is, however, a large field open for experimental investigation to show why Hyperpiesia should lead to such impaired resistance.

In view of the fact that pressor substances have been now demonstrated to result from putrefactive organisms acting upon proteins, it would be unwise to look

upon infection as a mere terminal event in Hyperpiesia, for it is possible that the so-called terminal infection is little more than the last and most effective manifestation of a bacterial invasion—the earliest manifestation of which was the production of hyperpiesis: here, again, the way is open for fresh experimental investigation. Till recently the only well-established effects of bacterial invasion of the body, other than the local reaction, have been the general anæmia produced, the fever, and hypopiesis. It is at least a singular fact that Hyperpiesia terminates so often by inflammation of serous tissues like the pericardium and pleura. Hæmorrhages are also common occurrences in the final stages of Hyperpiesia, with the result that the pericarditis and pleurisy are often hæmorrhagic in character. Hæmaturia, melæna, hæmatemesis, hæmoptysis, epistaxis are also common manifestations in Hyperpiesia, and possibly are further examples of the effects of bacterial invasion. Purpura and petechiæ are well-recognised effects of infection, and are not uncommon manifestations of the terminal stage of Hyperpiesia. Though it is not accepted as an established fact, there is reason to believe that hæmorrhages into the retinæ, which are common manifestations in the terminal stages of Hyperpiesia, are as much the ocular expression of the effects of infection as are other hæmorrhagic manifestations in the skin and mucous and serous surfaces.

Hypopiesis.—Several of the pressor charts shown clearly indicate that hyperpiesis may give place to hypopiesis; such change has been followed by death in a short or longer period. What is the cause of the hypopiesis? Hitherto it has been thought that hypopiesis is due to the depressor effects of bacterial toxins, which either by acting on the neuro-muscular junctions of the vaso-motor nerves have neutralised or superseded the effects of the pressor agencies previously producing hyperpiesis, or by acting on the cardiac muscle, producing degeneration in the muscle-fibres, have led to cardiac inefficiency and thus to hypopiesis. In recent years, experimental investigation has altered the current views upon the mechanism of hypopiesis: contrary to current teaching, falls of blood-pressure in the larger arteries may result from dilatation of the capillary system, independently of, and even in spite of, an increase of the tonus of the arterioles and independently of any action on the cardiac muscle. This extraordinary state of affairs has been most completely demonstrated experimentally, and a pure substance has been separated which is capable of producing such effects, namely, histamine. Histamine is a representative of a number of histamine-like agents all of which can produce this effect. Histamine and histamine-like substances are formed from proteins and pure histidine by the action of bacteria *in vitro*, and it is presumed also *in vivo*. The bacteria capable of producing these substances have been recovered from the healthy intestine. It is therefore possible that hypopiesis may be due to the effect of bacterial activity upon the body tissues or protein contents of the bowel, and results not from a vaso-motor loss of tone, but from dilatation of large areas of capillary vessels, with the result that a very large part of the blood passes into them.

Histamine-like substances may be formed during the autolysis of injured tissues or cells, although the evidence on this point is slender.

These investigations cannot but arouse the interest of the clinician, because he so frequently finds at post-mortem examination that large or small areas of cells, especially those constituting the parenchyma of various organs, have been cut off from their arterial supply by vascular occlusion, or the vitality has become so lowered as the result of toxins that they are necrosed. What becomes of these cells? They disappear and their place is taken by indifferent scar tissue. But what effects are produced by the products of disintegration of these cells, whether the disintegration is due to bacterial toxins or to autolytic ferments? The above observation can but encourage the belief that histamine-like bodies are produced, and if produced in sufficient quantities they must exert a profound influence upon the capillary vessels, leading to their dilatation, and as a result to falls of blood-pressure. Thus hypopiesis in turn is beginning to find a solution as well as those symptoms like "weakness" or "debility" which so often accompany it.

Hyperpiesic crises.—No phenomena noticed during the study of these forty-seven cases of Hyperpiesia have been so dramatic in character as the hyperpiesic crises already referred to. Within a few hours the blood-pressure has fallen through many millimetres, sometimes unaccompanied by symptoms, at others accompanied by most striking phenomena. The patient may develop convulsions, or suddenly become very collapsed, revealing a feeble running pulse, and may actually become unconscious, the symptoms passing off with recovery from the crisis. Many of these attacks may occur during several years. In some of the cases falls of pressure have been due to hæmorrhage from a gastric ulcer, but in others no such explanation has been found during life nor after death. What is the origin of this latter form of crisis? In the past they have been looked upon merely as the results of the accumulation within the system of metabolites which inefficient kidneys have been unable to excrete. But the fact that the kidneys have been found more damaged in other subjects who have not suffered from these crises, shows that the explanation is no longer satisfactory. It seems more reasonable to look for an explanation of hyperpiesic crises, which might well also be called hypopiesic crises, to the possible effects of the liberation of large amounts of agencies from the proteins of the body cells which have a histamine-like character, either from the effects of bacteria acting upon the cell proteins, or from the effects of the autolytic liberation of similar bodies from the protein of cells which have become necrosed as a result of arterial occlusion or of bacterial action. Whilst the hypopiesic crisis lasts these agencies are operating; when their effects pass off hyperpiesis is, or may be, re-established, the attendant symptoms passing off. In other words, it is possible that these crises are explainable in the same way as the "shock" observed in injured soldiers resulting from the damage of many cells, or the "peptone shocks" first described by Schmidt-Mühlheim when various unspecified cleavage products of protein digestion were experimentally injected: all are possibly produced by the liberation of histamine-like substances.

Convulsions.—The "shock"-like character of the crises just referred to may thus receive good explanation. But so far no explanation is to be found for these irritative effects, as opposed to paralytic ones, which are clinically described as fits or convulsions. The convulsive seizures met with in Hyperpiesia may be identical in detail with major epilepsy. The fact that epilepsy may occur without fits, as in the minor form, in no way has been held to be proof that epilepsy is not due to the effects of toxins upon the cortex cerebri: both forms of epilepsy are presumably toxic and the cortex cerebri is involved in each case, though with different effects—convulsive in one case and not in the other. So, too, in the coma and convulsions of Hyperpiesia the effects of toxic agents are different from reasons which must also remain speculative. Hyperpiesic convulsions and coma may be relieved by venesection.

Œdema.—Generalised dropsy, effusions into serous cavities and pulmonary œdema have been frequently met with in this series of cases, and apparently independently of bacterial invasion. How are such phenomena to be explained when it is known that the heart is acting more than sufficiently, when the kidneys may show no defect, or only slight defect not sufficient to cause a notable reduction of the output of urine? The experiments with the pure base histamine which may be taken to provide information on the group of other substances possessed of a histamine-like effect, again seem to offer help. It has been shown that histamine when experimentally injected not only causes a great dilatation of the capillary vessels, but also changes in the blood which indicate that plasma is lost from the blood by passing to extra-capillary sites, either from increased permeability of the capillary vessel walls, or from loosening of the lines of attachment of the capillary wall cells.

It is possible that when œdema supervenes in a case of Hyperpiesia, histamine-like substances are produced in the manner already described, and though there may be no contemporary fall of blood-pressure, plasma may leave the capillaries and give rise to œdema. This explanation of hyperpiesic dropsy is, however, at best a far-fetched one, and may even be quite wrong, because the dropsical fluid and the transudates met with are not so rich in proteins as blood plasma. There is, however, one point which encourages the belief that possibly histamine-like bodies are responsible for the œdema, and that is the rapidity with which pulmonary œdema occurs, sometimes to persist until death ensues and sometimes to pass off as quickly as it appeared. Clinicians are familiar with the rapid occurrence of œdema of the lungs, and with the sinister meaning of its occurrence when it does occur. It is possible, though far from proved, that histamine-like bodies may be liberated from the cells of the body as part of the process of their "molecular" death which ends in the "molar" death of the individual: if they are so liberated then œdema-like fluid would escape from the capillaries, producing the phenomenon which is met with in œdema of the lungs. The writer has seen death occur in this way in a girl æt. 18 years, suffering from aortic disease: respiration failed from intracranial pressure brought about by hæmorrhage into the frontal lobe: before the respiration failed the lungs were

free from œdema, but shortly after the respiration failed (ten minutes) the lungs were suddenly flooded with œdema, and probably this phenomenon was the actual final cause of death.

It is of interest that recovery may be brought about in hyperpiesic œdema of the lung by venesection.

Persistent or temporary hyperpiesic paralysis.—It is well known in cases of Hyperpiesia that hemiplegia or monoplegia may occur and be completely recovered from, or persist till death, and yet post-mortem examination reveals no organic cause for the paralysis : such palsies may recur several times : they present all the features of an organic lesion, including the characteristic changes in the reflexes : sometimes the paralysis affects sensory instead of motor areas of the cortex, so that the patient becomes quite blinded without any changes being discovered in the retina or brain. So far no experimental explanation is forthcoming for the occurrence of these palsies ; they can only be speculated upon and be thought to be toxic in origin ; the nature of such toxins and their mode of operation are quite unknown ; and there is no knowledge of why it is they can be recovered from even several times, beyond the supposition that the poisoning is small and can be recovered from.

Hemiplegia resulting from cerebral hæmorrhage is well known in Hyperpiesia, and is due to the rupture of cerebral arteries from weakness of the walls—the origin of which may be spirochætal or bacterial in nature.

Hyperpiesic albuminuria.—If the liberation of histamine-like bodies is ultimately found to occur in Hyperpiesia, then it does not seem impossible to explain albuminuria, sometimes slight in degree or transitory, even without any serious organic changes in the kidneys, as the effect upon the renal capillaries of these histamine-like substances, plasma escaping through the capillaries of the tufts and being diluted by the ordinary watery secretion of the kidneys.

There is also room for the theory that hyperpiesic albuminuria may be due to the effects of bacterial invasion of the tissues of the body at various sites, such as the gums, serous surfaces, etc., albuminuria being a common occurrence whenever such invasions occur, even in cases who reveal no hyperpiesis.

Anuria.—This is not common in Hyperpiesia, and when it has occurred in this series of cases, it has been found to be due to widespread death or loss of the kidney parenchyma, the result of arterial disease or of infection.

Neuro-retinitis.—Although œdema of the retinæ may be but the expression of the œdema which occurs sometimes in Hyperpiesia, no explanation is forthcoming of neuro-retinitis. It is clear from this study that it is not a mere function of albuminuria : the lessons learnt from the study of eclampsia show that it is toxic in origin, and that the toxin is pre-renal in its site of origin. It may in some cases, as is held by some authorities, be directly the result of the arterial change which is so common in Hyperpiesia, but it also occurs in the absence of arterial disease and is therefore probably toxic, and as eclampsia also teaches, if the toxic cause could be removed, would disappear. Mr. Percy Flemming informs me that he has seen albuminuric retinitis disappear in a non-eclamptic case.

Anaphylaxis.—The particular view of the mode of origin of the symptomatology of Hyperpiesia which has been developed in this study would not be complete without reference to the subject of anaphylaxis, or hypersensitiveness. The reasons are twofold: firstly, because of the appeal made to a pre-renal site and a protein origin for the production of Hyperpiesia and its attendant symptoms; and, secondly, because the symptomatology of anaphylactic shock shows so much parallelism with that of certain hyperpiesic phenomena, especially with regard to the feature of recurrence of certain of these phenomena. Thus in both conditions recurrent coma and convulsions may be met with; also recurrent tachypnœa, recurrent œdema of the lungs, recurrent falls of blood-pressure tachycardia, and recurrent asthmoid attacks.[1]

The complex of anaphylactic phenomena was originally discovered by Richet and Portier; these phenomena were produced as a result of the experimental reinjection of protein extracts of the sea-anemone: similar results occurred after the reinjection of the products of protein digestion and of the extracts of organs. The one desideratum for the production of anaphylactic phenomena (shock-like in their speed of development and in intensity) was that the protein body injected should be foreign to the animal experimented upon: bacterial proteins being foreign to an animal can produce the symptoms of anaphylaxis. If the cells of an animal are altered by the introduction of an alien proteid, a special amboceptor is produced within the cells and remains within the cell: if a fresh dose of antigen at a suitable interval is reinjected into the animal, it combines with the intracellular amboceptor and with complement; the conjunction of complement, amboceptor and antigen leads to the development of toxic material (the anaphylatoxin of Friedberger) and anaphylactic shock results: protein-cleavage has taken place in proximity to the contents of the cells and the phenomena of anaphylactic shock are produced.

Many of the phenomena met with in anaphylactic shock are closely simulated by those met with in the experimental injection of histamine, so that some observers have gone so far as to assume that histamine, or a body of histamine-like character, is one of the cleavage products of protein and is responsible for the picture of anaphylactic shock.

How can these discoveries be looked upon as giving an explanation of the various suggestively similar phenomena noticed in the hyperpiesic state?

The hyperpiesic patient is subject only to one form of anaphylactic influence. He may be infected by bacteria—a common experience: these bacteria may or may not give signs of local reaction like cellulitis, pleurisy, etc.; but the body may be subject to bacteriæmia without revealing fever or inflammatory reaction. Presumably the bacteria by their own disintegration give rise to alien protein-derivatives which render the body anaphylactic, so that when subsequent doses of derivatives of disintegrated bacteria of the same type re-enter the cells of the body anaphylactic phenomena occur, *i.e.* in view of what has been stated above, histamine-like effects are produced.

[1] *Lancet*, London, March 16, 1912.

In this way an explanation may be found for the subsequent symptoms of Hyperpiesia when once the particular hypersensitive state has been originated.

The reader is strongly advised to peruse the Herter Lectures delivered in 1919 by Dr. H. H. Dale on "Capillary Poisons in Shock," "Anaphylaxis" and "Chemical Structure and Physiological Action." He will find in these lectures many of the experimental facts upon which are based the particular applications which have been made of them in the above passages in the explanation of phenomena which hitherto have remained enigmatic. At the same time, the reader must be warned that in moments of pardonably intense interest in all that Dr. Dale has written the writer may have been tempted to pass from the realms of proved fact to that of speculative guess-work, despite the cautions Dr. Dale's papers impress upon their readers.

A further speculation is enforced upon the reader which may be found of greater interest by those who are not prepared to accept that the hyperpiesic subject is at all times suffering from bacteriæmia manifested or not by the usual clinical phenomenon of inflammation. To those who entertain such doubts, the above explanation of hyperpiesic symptoms will fail to appeal.

One of the greatest disappointments to the student of anaphylaxis who seeks to apply its lessons to clinical medicine has been that anaphylaxis has been demonstrated to be possible only when subtoxic doses of foreign proteins are introduced into the animal's body. To the question whether an animal can become anaphylactic to protein derivatives of its own cells the answer has always been that such a state of affairs has never been proven. That large areas of cells undergo disintegration is well shown in cases of cirrhosis of the liver and kidneys, or when a tract of tissue undergoes ischæmic necrosis by occlusion of the arterial supply by endarteritis, thrombosis, etc.: bacterial necrosis may also lead to the disappearance of large tracts of tissue. Do the products of such disintegration exert no action on the remaining tissues? If the surmise is correct that extensive trauma leads to "shock" owing to the liberation of the disintegration products of the cells damaged by the injury, there can be little doubt that similar effects should occur and recur in cirrhosis, occlusive arterial disease and bacterial necrosis of tissues.

Dr. D. Embleton[1] and the writer put this possibility to experimental test by the study of the hæmolytic character of the sera of animals which had undergone injection with the bloodless extracts of various organs removed from other animals of the same species, the argument being that this was a near approach to the absorption into the blood-stream of an animal of its own organs and tissue cells. Just as it has been found that the injection of the organs of a different species of animal causes an increase of the hæmolytic power of the serum of the animal injected, so also it was found that when animals were injected with the extracts of homologous animals the hæmolytic power of the serum was increased. Although most of the animals when experimented upon, even for several months, appeared to suffer neither from the original injection nor from the subsequent reinjections,

[1] *Brit. Med. Journ.*, 1909, Oct. 30.

some of them did, after reinjection, show marked tachypnœa and profound collapse. The frequency, however, of this occurrence was not enough to justify the conclusion that the anaphylactic state can be induced by the injection of an animal with its own protein, though it did appear that the animal's body was certainly altered by the procedure, as was shown by the increased hæmolytic power of the serum. It must therefore be confessed that when an attempt is made to find an explanation for the sudden attacks of loss of consciousness in cases of Hyperpiesia, often accompanied by feeble and rapid pulse and respiration and sometimes by convulsions, so far experiments, though very suggestive, have not shown that it is at present justifiable to consider that these attacks are due to the poisoning of the individual by histamine-like bodies derived from the disintegration of tissue or organ cells, as the result of the operations of anaphylaxis. If these phenomena are the result of the liberation of separate charges of histamine-like bodies, it seems that there are only two ways in which such liberation could take place, that is, either by the atrophy and autolysis of large numbers of cells from occlusive arterial disease, or from cirrhosis, or by the disintegration of large numbers of cells as the result of bacterial infection. That arterial occlusion or fibrosis and bacterial infection are likely causes of such an origin is shown by the frequency with which it is discovered in these series of clinical cases.

SECTION V

CONCLUSIONS

I NOW crave the indulgence of the reader and ask to be allowed to put together briefly the ideas formed as a result of this study. The study of this series of clinical cases enforces the view that Hyperpiesia results from the circulation in the body of some toxic agent, or agents, which are pressor in type, and which may be capable of producing the other toxic accompaniments of hyperpiesis. Facts have already been brought to notice which confirm the views of those who believe, as the result of clinical studies, that Hyperpiesia, even of very marked degree, may exist without any evidence that the kidneys are diseased, and for some years now post-mortem examination of cases recognised clinically as Hyperpiesia has shown that the kidneys may be normal, although in other cases they may be extremely altered in architecture, in size and in weight. It does not appear in some of the cases that the kidney is at all concerned in the development of Hyperpiesia, and yet on the other hand such a large number of cases in which hyperpiesis is present during life show such grave structural disease of the kidney that unless we are prepared to jettison much of the traditional teaching on the association of cardiac hypertrophy, hyperpiesis and kidney disease, we must accept that there is some intimate association, in certain cases at least of Hyperpiesia, between the hyperpiesis and the kidney disease. It does not appear to me to be unreasonable to think that in these cases possibly the hyperpiesis is directly due to the escape into the circulation of renin from the diseased kidneys, a substance which is found to be present in fresh extracts of the kidney, and even after autolysis of such extracts.

Then in those cases of Hyperpiesia in which the kidneys are found to be normal, the rise of blood-pressure, if toxic in origin, must be due to some other source of poison; it is possible that in these cases the pressor effects are due to the disintegration of proteins by bacteria (1) either as the result of the infection of various tissues which form so large a part in ordinary clinical medicine, or (2) as a result of the action of the flora of the alimentary tract upon protein foods. This speculation is supported by the knowledge acquired in recent years that when putrefaction occurs there is disintegration of proteins, with the liberation of clearly-definable (chemically and physiologically) pressor bodies such as isoamylamine, p-hydroxyphenylethylamine and phenylethylamine, and it is reasonable to suppose that these bodies absorbed into the circulation are capable of producing hyperpiesis. Further studies may reveal the presence of other pressor derivatives

of bacterial action in which the micro-organisms do not necessarily possess a putrefactive function. Further it may be possible to show that pressor bacterial derivatives may usurp the whole position and be shown to be the causes of the hyperpiesis associated with renal change, as well as of the hyperpiesis in which renal change is absent. The particular form, or shape, or size of kidney found in Hyperpiesia would then have little or nothing to do with the symptoms met with during life, other than those of anuria, and it may even be shown that the substances giving rise to Hyperpiesia may actually be responsible for the changes met with in the kidneys of so many of the series.

Supposing the above sketch proves to be correct, is there any justification for assuming that all the symptoms met with in Hyperpiesia also owe their origin to the agencies which are capable of producing hyperpiesis ? Reasons have already been put forward in support of this view, the position even being taken up that " uræmia " is practically a result of poisoning from the same sources, and is not due to any of the causes previously put forward, and that really the only absolute proof at the bedside that the kidney is gravely involved is suppression of the urine. Support for this view has been put forward in the review of the symptoms of cases of fatal Hyperpiesia, and by an appeal to the symptomatology of the disease known as Eclampsia of pregnancy, in which hyperpiesis is such a constant feature : indeed, the study of these forty-seven cases compels the writer to accept the view that Hyperpiesia and the Eclampsia of pregnancy are closely allied states ; both toxic in origin, both may be associated with signs and symptoms of renal disease (substantiated by post-mortem investigation) or not, both may be temporary and be recovered from, both may be permanent and lead to the death of the patient, and both may even show changes in the retinæ which are generally accepted as indicative of grave renal disease, but which, as post-mortem examination shows, should merely be accepted as indicative of a grave toxæmia, not necessarily of grave renal disease. The only material difference between the two states is that Eclampsia occurs in women in or about the time of pregnancy, and, further, that in Eclampsia the removal of the contents of the womb, venesection and saline infusion are amongst the most successful means of combating the toxæmia of this latter condition. If Eclampsia is toxic, Hyperpiesia is toxic. If Eclampsia can be cured by dilution or removal of the toxins, the same should be possible in Hyperpiesia. When it is discovered whether the toxæmia of Eclampsia is metabolic, bacterial, cellular or intestinal in origin, whether in the mother or in the fœtus, or in both, we shall be nearer the solution of the causes of the toxæmia responsible for Hyperpiesia.

So far, to date, no metabolite has been discovered which is pressor in type : all metabolites appear to be depressor. Up to the date of the discovery of isoamylamine, p-hydroxyphenylethylamine and phenylethylamine there were no derivatives of bacterial activity possessed of pressor action. The disintegration of the cellular elements of the body has not been shown to yield substances which are purely pressor in action ; but it has been shown that histamine which in its total effect is depressor in action has a dual power : it is pressor so far as the

arterioles are concerned, but depressor as the result of its action upon the capillaries, and this latter effect is the dominant one ; histamine may be developed in the living body when the cells of any injured tissue are cut off from their arterial supply and undergo autolysis. The only kindred conditions in which healthy cells could undergo autolysis within the living body are those in which the parenchyma of an organ like the kidney or liver undergoes disintegration by autolysis, when the blood-supply has been cut off by arterial occlusion (or interfered with as in the cirrhotic atrophy of the liver or kidney) or by thrombosis of small portal vessels of the liver as in Eclampsia (Schmorl). If sufficient histamine were yielded by autolysis and escaped the action of the liver, it is presumable that histamine "shocks" would occur—an explanation for the occurrence of the sudden falls of pressure, and possibly also for the more gradual ones that are seen when hyperpiesis gives place to hypopiesis. So far as the digestive processes are concerned there are apparently no observations which support the view that pressor bodies are produced other than those of Langstein already referred to.

Supposing the premise is accepted that in Hyperpiesia a pressor body, or pressor bodies, of proteid origin are liberated into the circulation and produce hyperpiesis and also produce the associated symptoms met with in what may be called pure Hyperpiesia, how can other phenomena met with in Hyperpiesia be explained? The way is open, because it has been frequently seen that cases of Hyperpiesia terminate from bacterial infection ; the bacteria themselves yield products of their disintegration which gain access to the system and render the body sensitive, hypersensitive or anaphylactic to subsequent charges from the same source and major or minor anaphylactic shocks occur, producing sudden death or gradual death from a process akin to septicæmia. If the question is raised, whether the above series of clinical cases provide examples of signs and symptoms akin to those of anaphylactic shock, the answer is that it does so so frequently that the probability that they are to be explained only by reference to anaphylaxis has been forced upon the writer ; for example, there have been several exquisite examples of the occurrence and recurrence of attacks of epilepsy, or coma, or syncope, or asthma, or œdema of the lung, or mono- and hemiplegia, of blindness without changes in the retinæ, of vertigo, of vomiting, headache, albuminuria, and of hyperpiesis.

As already stated, there are no animal experiments which enable us to understand how albuminuric retinitis is brought about ; but the study of Eclampsia has done much to fill up the hiatus, proving at any rate that it is a purely toxic effect which can be cured by removal of the cause of the Eclampsia.

The study of this series of forty-seven cases has resulted in various changes in the writer's conceptions with regard to kidney disease and to the alleged symptoms and signs of such disease, and also in the substantiation of views long held by various observers, but which have needed an inquiry, such as has been carried out in this study, to provide them with more solid foundations. Some of the conclusions arrived at may appear novel, and may appear to be insufficiently supported by experimental and other evidence. They will, however, it is hoped,

provide platforms from which further investigations to prove their correctness or not may be launched.

There would seem to be room for the introduction of a new caption in the list of diseases, namely for the condition which Sir Clifford Allbutt has entitled Hyperpiesia.

The distinctive feature of this disease is hyperpiesis. This appears to be the first clinical abnormality met with in Hyperpiesia. Hyperpiesia may pass off permanently or may recur. Whether in such cases the agencies causing Hyperpiesia can assume temporary activity and inactivity is not established by this study : a frequent cause for the disappearance of hyperpiesis appears to have been some infective process which acted as a source of neutralising depressor agents.

In this particular study investigations have been carried out on cases of Hyperpiesia in whom hypertrophy of the heart, especially of the left ventricular wall, has supervened. This cardiac hypertrophy may, it is stated, pass off permanently, or may recur. So far as this study is concerned, there is only slight evidence that the hypertrophy may pass off or be reduced, and then only as a result of a severe infection.

A very frequent occurrence is that the arteries like the brachial may become tortuous in those cases in whom Hyperpiesia has existed long enough to produce the deformity. So far as this study is concerned there is no evidence to show that this deformity passes off when once it has been initiated.

In the earlier stages of Hyperpiesia and even up to the time of death the patient may be quite free from symptoms and may look perfectly healthy.

The study of the later stages of this disease shows that it may terminate in cardiac defeat, the patient succumbing suddenly, or the disease may terminate with signs of pulmonary œdema ; or the patient may reveal signs showing that the nervous system is seriously involved, for example coma may ensue, also convulsions and evanescent or persistent palsies ; in the latter case coarse changes may be found in the central nervous system, or may be absent on naked-eye examination. The patient may succumb to changes indicating a gradual complete failure of the heart from muscle or valvular defect, for example dropsy and serous effusions may occur which resist treatment. In other cases the picture presented is that of renal disease, and may answer to the description given of the condition of granular kidney, and yet at the post-mortem examination such conditions of the kidney cannot always be established.

As is the case in other diseases, death may occur, not from Hyperpiesia already detected, but from some subsequently developing disease such as carcinoma of various organs, apoplexy, etc.

A common phenomenon in cases of Hyperpiesia ushering in death is terminal infection.

The terminal infection may be revealed by the observation of fever, but failing the occurrence of fever, or even of alteration of pulse-rate, its presence may be suspected when hyperpiesis gives place more or less rapidly to normal blood-pressure, and even to hypopiesis, or when petechiæ occur in the skin, or when

hæmorrhage occurs into the retina, or from mucous surfaces including that of the renal pelvis, or into the kidney substance.

Seeing that so many of the phenomena met with in the condition hitherto indicated by the word "uræmia" occur in cases of Hyperpiesia, the latter term should be used to describe such conditions. By doing so, an unproven but implied cause is replaced by a leading clinical manifestation, namely hyperpiesis. That such change is most desirable and necessary is shown by the fact that hyperpiesis has been shown to be a constant feature in this series of cases, being present not only in those cases who revealed "uræmia" and those changes in the kidney hitherto considered capable of producing "uræmia," but also in cases who revealed "uræmia" unassociated at the post-mortem examination with changes in the kidneys.

The study clearly proves that too much clinical reliance has been reposed in certain signs and symptoms which have been thought to indicate well-known types of chronic disease of the kidney, as established at the post-mortem examination. Such signs and symptoms have led to entirely erroneous opinions as to the actual condition of the kidneys.

It appears that the one clinical manifestation that can be relied upon to give a true indication of the capacity of the kidney to do its work is the power of this organ to secrete urine. Non-obstructive suppression of the urine has been shown in the first case of this series to have occurred only when all but a few renal cells were capable of discharging their function.

Probably no clinical manifestation is of more sinister portent than the retinal changes met with in cases who suffer from slight or severe albuminuria; the study shows that this serious sign, which so often is found to connote chronic disease of the kidneys, may occur without such association. The retinal change, like other less significant and accepted signs of chronic kidney disease, is also probably a toxic effect, the site of origin of which is pre-renal.

The Eclampsia of pregnancy is regularly accompanied by hyperpiesis, and death may occur in this disorder with little or no change in the kidneys of a severe and unrecoverable character. All the manifestations of "uræmia" alleged to be due to parenchymatous or chronic fibroid changes in the kidneys may be met with in such cases, including some of the retinal changes. Eclampsia may be entirely cured by the removal of the contents of the womb, and the kidneys, so far as can be ascertained, and the retinæ may completely recover from any disturbance they may have manifested. There can be no question that Eclampsia and its accompanying hyperpiesis are toxic in origin, and that such origin is pre-renal in site.

Hitherto too much attention has been paid to the study of those cases of Hyperpiesia which have revealed coarse naked-eye changes in the kidneys. More attention is needed in the biological study of the abnormalities of the blood in all cases of Hyperpiesia, not only in those in whom the kidneys appear to be diseased, but in those in whom, so far as can be ascertained, the kidneys are little or not at all damaged.

Further investigation is necessary for the elucidation of the mechanism by which cardiac hypertrophy, so constant a sign in Hyperpiesia, occurs when resistance short of actual occlusion is universally imposed on the arteries and arterioles.

Information is also needed as to the mode of origin of the papillœdema and retinal exudates met with in Hyperpiesia.

Considerable attention has been paid in this study to the discovery of sources of origin of pressor bodies which, operating on the arteries, could lead to the development of hyperpiesis.

Experimentally a pressor substance—renin—has been demonstrated to exist in the normal kidney, especially in the cortex.

It is possible that those cases of hyperpiesis which are proved to be accompanied by shrinkage of the kidney substance may owe the hyperpiesis to the entrance of renin into the circulation ; the hyperpiesis in these cases may be a nephræmic one. Support for this view may be found not only from the study of the cases in this series, but from the fact that in the early stages of acute kidney disease hyperpiesis is present.

Other pressor substances, however, must be found to explain hyperpiesis occurring in cases in whom the kidneys show little or no objective evidence of disease. Already it has been shown that definite substances like p-hydroxyphenylethylamine which are pressor in effect can be derived from the putrefactive action of bacteria upon meat. It is possible that similar changes going on within the intestinal tract are responsible for certain cases of Hyperpiesia. There are no suggestive experiments which throw light upon the origin of the toxic agencies which are responsible for the hyperpiesis met with in Eclampsia.

It is possible that all cases of Hyperpiesia, whether the kidney is gravely damaged or not, owe the hyperpiesis to some toxic agent circulated by the blood-stream but not derived from the kidney, the site of origin being for all of them pre-renal. If this is the case, then the changes met with in the kidneys, whether acute or chronic in character, may in turn owe their origin to poisonous effects arriving by the blood-stream, and the only significant contribution made by such damaged kidneys to the clinical picture may be non-obstructive suppression of urine and the very doubtful poisonous effects produced by retention of metabolites which cannot escape.

The well-known recurrent characters of many of the symptoms met with in Hyperpiesia call for explanation ; for example, why should coma, convulsions, various paralyses, dropsy, albuminuria, etc., occur, pass off and return again on subsequent occasions ? This may be due to poisoning by fresh doses of the agencies which are responsible for the disorder.

There is, however, another explanation possible, namely that the body has become sensitised by its invasion by protein derivatives, with the result that when fresh charges of such derivatives operate upon the body, they find it susceptible and lead to the development of periodic tachypnœa, tachycardia, pulmonary œdema, dropsy and effusions, syncopal attacks, coma, convulsions, palsies,

hypopiesic crises, etc. Kindred symptoms and signs are met with in what has been described experimentally as anaphylactic shock.

The most likely source of the invasion of the body by protein derivatives alien to itself is bacterial infection, and it is possible that the recurrence of the above signs and symptoms may be due to anaphylatoxins of such bacterial origin.

The phenomena of anaphylactic shock are closely parallel to those produced when histamine-like bodies enter the circulation, and it is possible that the above recurrent symptoms, like those met with after severe injury, are derived not necessarily from bacterial invasion of the body, but from the liberation in the body of material derived from its own cells.

An explanation of the recurrence of dropsy in Hyperpiesia in the absence of cardiac and renal disease is not yet established. The remarkable characteristic of histamine-like bodies that they can destroy capillary tone and lead to the loss of plasma through the capillary walls into the tissues is not without interest in this connection.

The frequent association of periods of hypopiesis which have succeeded the periods of hyperpiesis with terminal bacterial infection in this series of cases, has been frequently referred to. The more common effect produced by bacterial toxins is the lowering of the blood-pressure, and this may be explained by the effect produced when histamine-like bodies are liberated by the interaction of bacteria upon the body tissues.

THE THERAPY OF HYPERPIESIA

In the present state of knowledge of the cause of Hyperpiesia its treatment must be mainly, if not entirely, symptomatic.

Rest.—Of all the remedies tried, physical and mental rest have appeared to produce the most certain results. The charts shown provide several examples of the advantage of relying upon rest in bed, with little other help. The reason why rest in bed may not only lead to a diminution of the hyperpiesis, but to a cessation of unpleasant symptoms, must be that there is less demand made upon the circulation. That rest does not necessarily bring with it a fall of pressure is also proved by several of the charts shown, because during periods of the completest rest the blood-pressure has actually risen. Although it frequently happens that rest in bed does not materially reduce the hyperpiesis and does not prevent its intensification, yet symptoms frequently abate. To impose complete rest in bed upon all patients suffering from mere hyperpiesis is unnecessary; for it frequently happens that a subject showing hyperpiesis is particularly actively disposed in mind and body and is quite free from symptoms. When rest can be carried out completely, favourable results will be achieved more quickly.

When Hyperpiesia has been discovered, as it were by accident, in individuals applying for life insurance, or on medical examination before employment,

the medical attendant appealed to for treatment must be guided by circumstances as to whether he should insist upon a prolonged period of complete rest or not. If circumstances will admit of such treatment, and the patient is amenable, there can be no doubt that a period of increased rest is a fitting prelude to a life which in the future must be constantly more easeful. To those who object that the knowledge of the presence of hyperpiesis will cause anxiety to the patient, it must be said in reply that frequently the proper treatment cannot be secured unless the patient is fully informed of all the facts. It goes without saying that particularly nervous subjects should be shielded from too close a knowledge of the numerical measurement of the hyperpiesis, and it must be explained that a temporary variation between readings even of 20 or 30 mm., whether of increase or decrease of hyperpiesis, is immaterial. What is of favourable moment is the steady fall through several weeks to the normal level. Every advantage should be taken of the knowledge that sometimes Hyperpiesia is quite temporary, and that when the manifestation of hyperpiesis has passed off the patient is relieved of the accompanying symptoms. If it is discovered that the hyperpiesis persists even with prolonged rest in bed, it must be left to the practitioner to decide whether he should, or should not, reveal the fact of the permanent presence of hyperpiesis. It should be pointed out that though there is no knowledge whatever of the average duration of life when hyperpiesis has established itself, or what is the average period required for the development of the symptoms when once hyperpiesis is established, there is room for a degree of optimism when it is discovered that the blood-pressure is raised. More especially is this the case when it is found that the individual concerned looks healthy and is comparatively, or entirely, free from symptoms. It is not always wise, in order to secure the obedience of the patient, to point out the risk in cases of accidental or other discovery of hyperpiesis of the occurrence of apoplexy, hemiplegia, etc., because the number of cases of Hyperpiesia to be met with in men and women of about middle age or more must be very considerable, judging at least by the routine examination of patients and candidates for insurance, and yet the frequency of apoplexy in such subjects is comparatively small. There can be no doubt whatever that when hyperpiesis is found to be associated with anæmia, intense fætor of the breath, dyspnœa, cardiac embarrassment, dropsy, etc., then rest in bed should be insisted upon; naturally such cases would more readily conform. When a patient appears before the practitioner merely revealing hyperpiesis, being in every other way apparently in good health, it is sufficient to try and secure more rest in the hours not devoted to business: in the winter, arrival at the office an hour later than usual may be helpful; the spending the whole of the week-end, or the greater part of it, in bed will help to postpone the development of further symptoms. When the practitioner is in doubt as to whether the patient is suffering from permanent Hyperpiesia or not, rest in bed would provide means of clearing up the problem: if the blood-pressure becomes normal within four or five days, it may be that the individual is merely suffering from what may be spoken of as the "nervous" form of hyperpiesis: more especially would this be probable if

the hyperpiesis were found to be unaccompanied by evidence of cardiac hypertrophy, tortuosity of the arteries, albuminuria, retinal change and the other manifestations met with in the later stages of Hyperpiesia. Even if the case does prove to be one merely of evanescent hyperpiesis of nervous origin, a more restful life, short of causing great inconvenience to the patient, can do no harm, and may be a means of preventing such evanescent hyperpiesis becoming one of permanent hyperpiesis. It will be remembered that Cases 18, 21 and 27 of the fifty cases considered in this study have had to be eliminated because the evidence of hyperpiesis was slender, and because post-mortem examination did not reveal any hypertrophy of the left ventricle of the heart : the hyperpiesis in these cases was possibly of nervous origin. With regard to cases of nervous temporary hyperpiesis, it must not be inferred that they never become cases of Hyperpiesia.

For practical purposes the development of left-sided cardiac hypertrophy may be regarded as the " hall-mark " of the permanent or much more prolonged hyperpiesis, *i.e.* of Hyperpiesia.

Dieting.—Much controversy has centred around the subject of the diet suitable for a hyperpiesic subject : a diet rich in carbohydrates should be avoided in order to reduce flatulence, and a diet rich in extractives should be excluded in those cases in whom the kidneys are gravely disturbed. Should the patient be free from symptoms and merely show the earlier signs of Hyperpiesia, it is sufficient to leave the patient to choose his dietary just so long as he selects what may be reasonably called simple foods. It does not seem wise to cut down the protein elements of a diet because the patient is passing albumen : indeed this phenomenon should be a call to supply, if anything, extra protein food. If it is found that headache and dyspeptic manifestations are controllable by a simple diet consisting mainly of milk, or of eggs, or fish in part, there can be no reason on the other hand to insist upon a more richly protein diet. Alcohol, tea and coffee in moderation exercise no harmful effects upon the disease. Seeing that the hyperpiesic subject may be free from any symptoms, and seeing that next to nothing is known of how to control the agencies which are producing hyperpiesis, it seems wrong to insist upon this, that or other extreme form of dietary. It is more reasonable to leave the patient to his own choice just so long as he exercises moderation.

Supposing early symptoms have developed which indicate the onset of the more serious complications of hyperpiesis, such as anuria, cardiac defect, dropsy, drowsiness, etc., it is advisable to place the patient upon a rigorous milk dietary, allowing 3 to 4 pints a day. This, combined with rest in bed and purgation, leads in some cases to disappearance of the symptoms, and then the future dieting of these patients should be based upon the knowledge that restriction exerts favourable effects. If the above features persist, then a very restricted dietary should be maintained. The dropsy may yield to the use of diuretics such as liq. ammon. acetatis, theobromine, diuretin or theocin.

Supposing a case of Hyperpiesia has undergone prolonged rest in bed with disappearance of symptoms, if not of hyperpiesis, work may be resumed gradually, and continued with if the symptoms do not recur ; but such a patient should be

kept steadily under observation. The question must be raised as to what amount of exercise should be allowed to these patients. It is a good maxim to lay down that they should take exercise short of producing such symptoms as cardiac pain and marked, or persistent, dyspnœa. Games involving severe muscular effort should be forbidden, as well as the unnecessary ascent of hills or staircases, or walking against a "head"-wind. Exercise must be allowed daily, and walking on the flat for a reasonable distance should be encouraged. There can be little doubt that when the patient is kept in bed, massage and gentle passive movements must be made use of to replace voluntary exercise. Such treatment does not appear to affect the blood-pressure unfavourably to any material extent. With regard to the cutting off of more vigorous exercise and game-playing, no absolute rule can be laid down, because there are some subjects who reveal hyperpiesis and are able to play golf and tennis quite vigorously without any symptoms occurring. Such patients may object to have this amount of exercise restricted and the medical attendant must permit it until unfavourable symptoms arise, or until examination shows the progressive intensification of objective changes. The use of tobacco is permissible.

Purgation.—The use of Epsom salts or Glauber's salts, taken before breakfast in such quantities as to produce one or two stools a day, is advisable. Intestinal putrefaction should be controlled by the use of calomel in fractional doses of such size as not to cause colic or other symptoms in susceptible subjects : the calomel may be given at night or three times a day after food. This should be a routine treatment, but if symptoms of drowsiness suggestive of impending coma occur, then castor oil should be freely used.

Baths.—If the patient relishes tepid or warm baths, he should be encouraged to take them regularly. In the same way it will be found that some patients enjoy Turkish and radiant heat baths, and when this is the case they may be used daily or two or three times a week. The radiant heat bath is a very convenient form, for it can be made use of in the patient's own home : it may be found by preliminary trial that unpleasant symptoms like headache may be produced by their use. It would be wrong in such cases to insist upon this method of treatment, for there is no proof that the treatment eliminates the poisons concerned in the disease, or in any way controls the mechanism by which dropsy can be developed. Hot air baths do not lead to the permanent fall of blood-pressure. The sole reason for using hot baths is that they relieve some patients from some of their symptoms, notably headaches, though as already mentioned they provoke them in others. It is probably more satisfactory to the patient to live in a well-warmed house ; quite possibly too cool an atmosphere contributes still further to a maintenance of high blood-pressure.

Choice of climate.—Residence in mild, temperate and warm countries is certainly to be preferred to residence in colder latitudes. Those who cannot winter out of England should reside at the milder west and south-west coasts. But here, again, as so often happens in the discussion of treatment, the temperamental peculiarities of the patient must not be disregarded. Some hyperpiesic subjects,

contrary to expectation, feel better in the winter than in the summer, and some prefer the east to the west coast.

Symptomatic treatment.—Usage alone sanctions the routine prescription of potassium iodide, of potassium nitrate and the various nitro-compounds. The use of such remedies may, however, prove unacceptable to the patient, and it would in such cases be undesirable to insist upon them. It will be frequently found that the nitro-compounds are helpful in relieving the angina-like pains. Headache is often relieved by the use of aspirin, phenacetin, bromides, etc. Insomnia is only too frequently a serious symptom, and should chloral hydrate, the bromides, trional, chloralamide, etc., fail to produce sleep, then paraldehyde, hyoscine and opium derivatives should not be spared.

No sign or symptom will prove more difficult than those which may be attributed to cardiac failure or defeat. The medical attendant should therefore maintain an open mind as to the use of digitalis and its allies and diuretics. It is true that at first sight the use of digitalis in a case already showing hyperpiesis seems doomed to failure and worse, but its diuretic effect and its power in certain cases of rendering the heart regular in rhythm may outweigh all theoretical objections. The occurrence of convulsions may require the use of hypodermics of morphia, of venesection or of spinal puncture. If coma threatens and cannot be met by the use of aperients such as croton oil or castor oil, venesection may again be of the greatest use. The well-known efficacy of bleeding by venesection or venepuncture in œdema of the lungs renders this form of treatment the standard one for such conditions.

Dropsy or serous effusions cause very considerable difficulty. If they fail to respond—as they too often are found to do—to the effects of diuresis and diaphoresis, then in the case of pleural effusion and ascites relief may be given by tapping the chest or the abdomen. Dropsy of the legs should not be relieved by the use of Southey's tubes, acupuncture or malleolar incisions, for although such methods are immediately efficacious, too often cellulitis results, despite the most meticulous care taken to prevent it.

Asepsis.—There can be no doubt that the risk of septic infection in cases of Hyperpiesia is a real *bête noire*. Every means should be taken to remedy gingivitis, and to prevent septic infection generally, for, as this series of cases shows, infection too often is the prelude of the sudden or slow demise of the patient. Should extraction of the teeth become necessary to cure gingivitis, then the extraction should be gradual, only a few teeth being removed at a time. General anæsthetics appear to be well borne by hyperpiesic subjects. When once severe anæmia has become established, as a result of infection, it is difficult to remedy it.

Life Insurance.—As this study has shown, men and women appear to show hyperpiesis which is apparently due to excitement only. It is therefore unwise to exclude from insurance or to load any individual who on the occasion of examination for life insurance shows hyperpiesis. If, however, a single reading of high tension is accompanied by signs of cardiac hypertrophy and vascular change, its significance is established. If hyperpiesis is the only discoverable clinical

sign, the proposer should have readings taken of the blood-pressure before rising after a night's rest, and if possible on more than one occasion. The persistence of a high reading under such circumstances should lead to a loading and (or) shortened period of endowment. The presence of albumen should in such cases arouse further caution: the urine may be free from albumen if the sample is one passed in the early morning after a night's rest: in such a case no extra apprehension need be felt. If albuminuria can be removed by the cure of septic foci, then the case should be looked on as one of mere hyperpiesis and loaded accordingly. If, however, albumen persists as well as the hyperpiesis, then such a case should be declined, not because the presence of albumen necessarily indicates kidney disease, for that fallacy has been unmasked, but because albuminuria is some measure of the greater severity of the toxæmia which is causing the hyperpiesis in such a case, or may mean that there is some hidden focus of septic infection. The presence of albuminuric retinitis should remain, as it has done, an absolute bar to insurance, because even though albuminuria may in such a case be slight or occasional only, retinal change renders the outlook so much more serious.

Syphilis.—If a hyperpiesic patient is the subject of syphilis, radical treatment should be instituted with the object of trying to prevent the weakening of the arterial walls which results from this disease. The risk of rupture of blood-vessels, already weakened by syphilis, is greater in the condition of hyperpiesis than when the blood-pressure is normal.

General anæsthetics.—Those who are the subjects of Hyperpiesia appear to me to stand the effects of general anæsthetics very well.

Operation for glaucoma.—With regard to the operation of iridectomy for glaucoma in a patient also suffering from Hyperpiesia, I think a preliminary rest in bed for a fortnight, with the usual dietetic and medicinal treatment, is worth trying, for it may be successful in reducing the blood-pressure, thereby also minimising the risk of intra-ocular hæmorrhage following upon the operation.

The reader will find in Sir Clifford Allbutt's work on *Diseases of the Arteries* (vol. ii. p. 80) full references to other measures which have been found helpful in the treatment of Hyperpiesia.

INDEX

[1] Cases 2, 16, 22, 24, 26 (?), 29, 35, 36, 37, 41, 43 and 45 also had valvular disease of the heart ; Cases 6, 43 and 50 had apoplexy ; Cases 12, 13, 30, 37 and 48 revealed carcinoma ; Case 34 had a meningeal haemorrhage. In these cases, therefore, the symptoms found were not necessarily due to pure Hyperpiesia.

Date Due
